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THE INCIDENCE AND HISTOLOGICAL TYPES OF PULMONARY CARCINOMA, WITH COMMENTS ON SOME FALLACIES AND UNCERTAINTIES.[1]

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THE main object of this paper is to examine critically two prevalent assumptions about lung cancer, the truth of which most recent writers on the subject accept as established, either openly or by implication. These assumptions are: (i) that the increasing number of recorded cases is a result, not only of improved diagnosis, but also of a real increase in the incidence of the disease, and (ii) that lung carcinomas can be subdivided without difficulty into several distinct histological types, and that these differ in their ætiology and behaviour. Let us examine each of these propositions in turn.

Is Carcinoma of the Lung Increasing in Frequency?

Whereas up to the second or third decade of this century carcinoma of the lung was regarded as a relatively rare disease, it is now recognized as one of the commonest malignant tumours. In 1900 the annual death rate attributed to lung cancer in England and Wales was eight per million persons; by 1925 it had risen to 20 per million, by 1950 to 278 per million, and by 1952 to 321 per million—that is, 40 times the rate for 1900 (Doll, 1953). Is this very remarkable increase real, or is it a result mainly or wholly of improved diagnosis? Let us look first at some lung cancer records of the last century, and then at those of the early and later decades of this century, trying to assess the degrees of precision of diagnosis at different periods, and also perhaps descrying some evidence of the real frequency of the disease during the earlier periods.

Lung Cancer Records Before 1900.

I happen to possess in my library a single volume of the *Transactions of the Pathological Society of London*; it is Volume 39 for the year 1888. I looked through it for reports of possible cases of lung cancer, and I discovered no less than seven necropsy records in which the descriptions enable us to make a confident retrospective diagnosis of bronchial carcinoma, although only one of these cases was so diagnosed at that time. Review of these seven cases is very instructive; the relevant facts about them are as follows:

[1] Read at the Cancer Congress of the Anti-Cancer Council of Victoria on August 23, 1960, at Melbourne.

1. Under the title "A Case of Cystic Growths in the Cerebellum and Right Adrenal", Turner described the necropsy findings in a man, aged 44 years, who had suffered from headache and vomiting and had displayed signs of cerebellar disease for 18 months. Two separate hæmorrhagic and cystic tumours were found in the cerebellum, the right adrenal gland was replaced by a tumour the size of a fist with areas of necrosis and a central cavity containing "gelatinous matter", and there was "pneumonic consolidation of the upper part of the right lung". Microscopic examination of the cerebellar and adrenal tumours showed that the growth consisted of "a fine reticulum, indistinct and cloudy in the sections, in which are round and elongated oval nuclei of considerable size". The "pneumonic" lung was not examined microscopically, and no information is given about its bronchi. Turner commented that the "cerebellar tumours may have been secondary to the large and more fibrous abdominal growth, being of a very similar structure, and multiple primary growths in the brain being especially rare". In retrospect, however, we can have little doubt that this was a case of bronchial carcinoma, probably of the right upper lobe bronchus and probably oat-celled, with metastases in the brain and adrenal gland.

2 and 3. Under the title "Two Cases of Mediastinal Cancer", Handford reported (*a*) a large tumour involving the mediastinum and left lung, with metastases in the cervical lymph glands and the liver, in a man, aged 45 years; microscopically this was judged to be an "alveolar scirrhous carcinoma"; and (*b*) a tumour of the mediastinum and hilum of the right lung, with extensive involvement of the pleura and metastases in the humerus, muscles and kidneys, in a man, aged 40 years. Microscopically this was seen to be composed of cells of irregular size and shape with an alveolar arrangement in parts, giving appearances which "pointed to carcinoma". Commenting on these two cases, Handford wrote: "The majority of mediastinal growths that have been described recently have been sarcomata. I think there can be no doubt that the two cases I have brought forward are true carcinoma." However, he was doubtful "whether it commenced in the bronchial glands, bronchial mucous membrane, or in the connective tissue", and the legend to his figure describes the tumour as "carcinoma originating in the mediastinum and involving the lung".

4 and 5. Under the caption "Malignant Disease of Bronchial Glands" (that is, lymph glands) Pitt described the following cases: (*a*) a "sarcoma of bronchial gland invading bronchus" in a man, aged 70 years, a tumour measuring 1·5 in. by 1 in., close to the left main bronchus, "which it had invaded slightly, so as to form a small swelling on the inner surface"; and (*b*) a "carcinoma of bronchial gland", growing around the right main bronchus and obstructing it "so that it would just admit a probe", with metastases in the left lung and the cervical lymph glands, in a woman, aged 67 years. Microscopically this second growth was judged to be a large-cell scirrhous carcinoma, which Pitt considered had probably "originated in the lymphatic gland, but . . . the lung might have been the starting point".

6. Under the diagnosis "Primary Cancer of the Pleura", Pitt also described the case of a woman, aged 61 years, with a year's history of cough, shortness of breath and clubbing of the fingers. Necropsy revealed an extensive growth of the left pleura "capping over the upper part of the lung" and extending "round the bronchi near the trachea and round one branch of the pulmonary artery", and metastases in many thoracic, cervical and abdominal lymph glands, as well as in the pericardium, the liver and the submucosa of the small intestine. Microscopically many parts of the tumours showed well-differentiated columnar-cell adenocarcinoma. Yet Pitt mistakenly supposed (as have many later workers) that "the appearances presented in the *post-mortem* room of a uniform dense infiltration of the whole of the parietal pleura by growth pointed very strongly to its being the primary seat whence the disease had spread over the apex of the lung. . . . Every portion of the body was carefully searched for the primary source, and it appeared conclusive at the *post-mortem* that the pleura was the primary seat. When on microscopical examination the growth was found to be cylindrical-celled epithelioma it was strongly suggestive of a primary growth elsewhere." Pitt admitted the possibility that the source might be "the mucous glands of the bronchi", but thought this unlikely because "the growth did not invade the root of the lung, while the growth at the apex of the left lung, and the small nodules in the right, were quite superficial, and did not affect any bronchi so far as one could judge". I have cited this case at some length, not only because it is so fully and accurately described, but also because it exemplifies so well a mistake in pathological diagnosis which has been made by many later pathologists, even to the present day.

7. Under the title "Case of Multiple Cancerous Tumours, Many of them Cystic, in the Lungs, Brain, Bones, etc.; the Primary Tumour Probably in the Lung", Coats gave a particularly full and excellent account of a case of bronchial carcinoma in a boy, aged 17 years, who for seven months before his death had suffered from headache and vomiting, and who had developed metastatic growths in several bones. Necropsy showed a primary tumour of the right lung involving the major bronchi, with metastases in the hilar lymph glands, both lungs, many bones, many parts of the brain, the liver, the pancreas and the peritoneum. Microscopically it was seen to be a well-differentiated adenocarcinoma with mucus-secreting goblet cells in some areas; and Coats inferred that it had arisen from the mucous glands of the bronchial wall. Coats also drew special attention to the fact "that during life the symptoms pointed almost alone to the state of the brain and of the bones", pulmonary symptoms being surprisingly absent.

Thus, in this volume for the year 1888, we have necropsy records of seven cases of bronchial carcinoma, only one of which, however, was correctly identified (that of Coats), the others being variously misdiagnosed as mediastinal tumour, sarcoma or carcinoma of bronchial lymph glands, primary cancer of the pleura and primary adrenal tumour with cerebellar metastases. These are mistakes which we now know to have been made very frequently with bronchial carcinoma. Two points of great significance regarding the incidence of bronchial cancer are indicated by these 1888 records: (i) the fact that no less than seven necropsy reports of this disease were brought to the notice of the society in one year strongly suggests that the disease was far from rare; and (ii) the fact that only one of the seven death certificates would have borne the diagnosis "carcinoma of the lung", in spite of necropsies having been performed, certainly means that for all cases of the disease, including those in which no necropsy was performed (probably none of which would have been designated "carcinoma of the lung" on the death certificates), the proportion of correct diagnoses on the death certificates would have been very much lower than one in seven. Since this one volume of the *Transactions of the Pathological Society of London* proved so instructive, I decided to examine other volumes for the light they might throw on the frequency and misdiagnosis of pulmonary cancer at that time. I abstracted all the relevant cases from Volumes 32 to 51, which covered a period of 20 years (1881 to 1900), and the findings are briefly as follows.

The 20 volumes contain necropsy reports of 34 cases which were certainly, or almost certainly, cases of bronchial carcinoma; in 31 cases in which the sex is stated, this was male in 24 and female in seven—a ratio of 3·5:1·0. The diagnoses made were as follows: mediastinal tumour, 12 cases; carcinoma of the lung, 8 cases; other tumours of the lung, 4 cases; abdominal (usually adrenal) tumour, 6 cases; pleural tumour, 2 cases; tumour of the brain, 1 case; disseminated cancer, 1 case.

Two of the reports just cited are worth noting, since they give further indications of the prevalence of pulmonary carcinoma in those days. Moore (1884), after describing a case of "endothelioma" of the mediastinum (an obvious bronchial carcinoma with adrenal metastases), wrote: "In the last 4 years I have examined *post mortem* six other cases of new growth in the mediastinum." Handford (1890), after describing and correctly identifying a case of carcinoma of the lung in which pulmonary symptoms had been absent, stated that in the prevous year he had seen three necropsy cases of this disease, and in the current year another one, as well as two other probable cases which, however, did not come to necropsy. He added: "From the fact that true carcinoma of the lung or its root is very rarely large in bulk, and from the variety of symptoms, I feel sure that many cases die undiagnosed, and that the affection is far more common than is supposed."

Lung Cancer Records, 1901-1930.

It would be tedious and unprofitable to attempt to examine pathological records for this period in the same way as for the earlier one. It was during the first three decades of the present century that pathologists generally became aware of the real frequency of bronchial cancer, of its diverse and misleading clinical manifestations and of its variable and often "sarcoma-like" histological appearances. Barnard's paper first identifying those tumours of the mediastinum formerly known as "oat-cell sarcomas" with bronchial carcinomas was not published until 1926, and American recognition of this fact came in 1930 (Karsner and Saphir). Since "oat-cell carcinomas" form roughly one-half of all bronchial cancers in most series, we may infer that up to about 1930 roughly one-half of all bronchial cancers had escaped recognition from this cause alone. I recall that, here in Melbourne, we students of pathology in 1920 were taught that there was a class of "alveolar sarcomas" and that the mediastinum was an important site of such growths. However, ten years later, three years' experience of necropsies at the Austin Hospital, Heidelberg, had taught me that intrathoracic "alveolar sarcoma" was bronchial carcinoma, and also that pulmonary carcinoma, far from being a rarity, was quite a common disease. It is of interest that, even as late as 1940, MacCallum, in his splendid "Text-book of Pathology", depicted and discussed "alveolar sarcoma" and stressed the difficulty or impossibility of distinguishing it from carcinoma.

Statistical studies of lung cancer as a cause of death in Great Britain during these three decades are provided by Bonser (1928 and 1934), by Passey and Holmes (1935) and by Kennaway and Kennaway (1936). Bonser's analysis of necropsy records in Leeds showed that over a period of 41 years there had been no increase in intrathoracic cancers, with respect either to the total annual number of necropsies, to the number of cancer necropsies or to the total admissions to hospital. Passey and Holmes examined the necropsy records of 16 large British hospitals for the period from 1894 to 1928, calculating the number of intrathoracic cancers appearing in the autopsy room as a percentage of the total admissions to hospital. On these estimates, eight of the sixteen hospitals showed no increase of intrathoracic tumours over this period, three showed indeterminate results and five showed a definite increase; but in each of these five hospitals there were special circumstances—special chest clinics, pathologists or clinicians with a particular interest in chest diseases—which could have accounted for the increase. Kennaway and Kennaway studied the numbers of death certificates issued yearly for cancer of the lung in males in England and Wales for the 12 years from 1921 to 1932. These increased steadily from 361 in 1921 to over 1500 in 1932—a fourfold increase. During this period necropsies were performed on 25% of patients certified as dying of lung cancer. The Kennaways commented that "Improvements in diagnosis must have led to the detection of a larger proportion of the existing cases of lung cancer; whether there has been an actual increase in these cases cannot be decided from the data presented here".

It is impracticable to review here more than one or two of the European and American writings on the subject; and I shall mention only Sitsen's German study (1935), from which he concluded that there was no proof of any real increase in the incidence of lung cancer, and that of Steiner (1944), who, after analysing the annual records of the University of Chicago Department of Pathology for the period 1902 to 1941, concluded that these showed only a slight apparent, but no real, increase in the incidence of the disease.

Of the many papers that might be cited from the literature of the first three decades of the century, illustrating the frequency of diagnostic errors in lung cancer, I shall mention only two, one British and one American. Simpson (1929) analysed the records of 139 necropsy cases of carcinoma of the lung and found that the clinical diagnoses had been incorrect in 66 cases (48%), in 11 of which the erroneous diagnosis was due to cerebral metastases. Fried and Buckley (1930) reviewed 37 necropsies in cases of pulmonary carcinoma; 15 of these subjects had cerebral metastases, and in 11 of these 15 cases the clinical diagnosis had been "primary cerebral tumour".

Taking into account the frequent errors of clinical diagnosis, along with the correction of some of the former major errors of pathological diagnosis which we discussed earlier, it is, I think, quite probable that the fourfold increase in registered deaths from lung carcinoma, which took place between 1900 and 1930, was attributable mainly, perhaps wholly, to better diagnosis.

Lung Cancer Records, 1931-1960.

During these three decades, the number of deaths attributed to lung cancer in England and Wales has shown an even greater increase. The actual number of registered deaths in 1929 was 1208; in 1950 it was 12,241—a tenfold increase in the two decades. However, expressed in rates per million of population and with due allowance for changes in the age and sex composition of the population, the increase in the two decades 1931 to 1950 was not tenfold but fivefold (Doll, 1953). Can the whole of this great recent increase be attributed to better diagnosis? Or must we assume that in addition there has been a real increase in the number of lung cancers? Most recent writers on the subject have concluded that there has been a real increase, and that it is probably substantial (Bonser, 1938; Kennaway and Kennaway, 1947; Heady and Kennaway, 1949; Daff *et alii*, 1951; Doll, 1953). For the detailed pros and cons I must refer you to these papers; all I can do here is to focus attention on some of the main points.

As we have already seen, the necropsy records of large British hospitals did not show any convincing evidence of an increased frequency of lung cancer during the first three decades of this century. But during the next two decades, many of the same hospitals did show a considerable increase in the percentage of lung-cancer cases in their necropsies (Heady and Kennaway, 1949; Daff *et alii*, 1951). Whereas in the early years of these two decades lung cancer accounted for about 15% of cancer necropsies, in the later years it accounted for between 20% and 30%—more than a 50% increase on the earlier proportion. However, not all large hospitals showed an increase in this period; for example, Bryson and Spencer (1951) analysing 866 necropsy cases of bronchial carcinoma at the Archway Hospital, London, for the years from 1936 to 1947, found that the percentage of cancer necropsies in which death was found to be due to pulmonary carcinoma remained almost constant, that is, between 25% and 28% of the total number. However, supposing that the Archway Hospital was for some unknown reason exceptional, and that in British hospitals in general the proportion of cancer necropsies in which death was found to be due to lung cancer was 50% greater in the 1940's and 1950's than in the 1920's—that is, three cases instead of two—this is a very moderate increase compared with the tenfold rise in the number of lung-cancer death certificates in the same period. On which of these two very different rates of increase are we to rely as an indication of the real trend in the frequency of the disease? Or is the truth that we can rely on neither? If we assume that the increase in registered deaths more nearly indicates the real increase—that is, that for every one case of lung cancer which existed in the 1920's and 1930's ten cases existed in the 1950's—then, clearly, very few of this greatly increased number must have reached the autopsy rooms, for the proportional increase there was in fact very much less. But this is not the case; there is clear evidence that the proportion of registered cases of lung cancer which came to necropsy in recent years is nearly the same as 20 years earlier; the Kennaways' 1947 analysis of death certificates showed that in both the period from 1921 to 1932 and that from 1933 to 1938 the percentage of cases in which necropsies were performed was the same—namely, 25—and there is no reason to suppose that the percentage has greatly declined more recently. If, on the other hand, we assume that the modest increase of lung cancers in the autopsy rooms (an increase in the ratio of 3:2 in the twenty-year period)

more nearly indicates the real rate of increase in the incidence of the disease, then clearly we must infer that of the tenfold increase in the registered deaths, 9·5 tenths of the increase was due to better diagnosis. And it becomes pertinent to ask, if 9·5 tenths of the increase is attributable to better diagnosis, why not the whole of it?

Mistakes in Clinical Diagnosis.—More diagnostic mistakes have been made in lung cancer than in any other kind of malignant disease; and general appreciation of this fact has been a development mainly of the last three decades. In the 1948 edition of my "Pathology of Tumours" I recorded an investigation which I carried out at the Alfred Hospital, Melbourne, during the years from 1936 to 1944, comparing the clinical and post-mortem diagnoses in 1000 consecutive cancer necropsies, including 71 (later increased to 84) cases of carcinoma of the lung. Correct clinical diagnoses were recorded in 49 of the 84 cases (58%); tumour was diagnosed, but the primary site was wrongly diagnosed or uncertain in 19 cases, in 17 of which secondary growths had caused the main symptoms (in the brain in five cases); and diagnoses of various non-neoplastic diseases, mainly of pulmonary infections, had been made in 16 cases. Thus, in 42% of the series, the diagnosis of lung cancer would not have appeared on the death certificates. Between 1948 and 1957, Teir and Koivuniemi (1959) carried out a similar investigation in Helsinki; of 102 cases of lung tumours, 56 had been quite correctly diagnosed, in 19 a tentative correct diagnosis had been made, and the number of wrongly diagnosed cases was 27 (26%). In Great Britain, Fullerton (1956) gave the following figures from a large London hospital for the three years from 1950 to 1952: total number of deaths, 1218; total number of necropsies, 753 (61% of deaths); carcinoma of lung suspected before death and confirmed at necropsy, 37 cases; carcinoma of lung unsuspected before death found at necropsy, 22 cases (37% of lung cancers). Eliman (1953), also of London, although giving no numerical estimate of misdiagnoses, recorded many cases illustrative of the great variety of misleading manifestations of the disease and the mistakes in diagnosis which they cause. The Registrar-General, in his commentary on his "Statistical Review of England and Wales" for 1956, gave an account of 87 cases in which a diagnosis of pulmonary carcinoma was made either before or after necropsy. Of the 87 cases, 53 (61%) were correctly diagnosed clinically; in 23 cases (26%) the pathologist discovered clinically unsuspected lung cancer; and in eight cases a clinical diagnosis of carcinoma of the lung was incorrect. There were thus 79 actual cases of the disease, of which 23 were not diagnosed (29%). The Registrar-General's own comment is worth quoting. He wrote that carcinoma of the lung "is still considerably under-estimated despite the increase in diagnostic facilities and in the awareness of the disease". I am interested to note in passing here the 9% of cases (in my own series it was 12%) in which a positive clinical diagnosis of lung cancer was made when it was not present—a mistake which, we may be sure, rarely or never happened in the earlier decades of the century, and which indicates the increasing awareness of the disease on the part of clinicians.

In summary, then, during the last three decades, in large metropolitan hospitals lung cancer still escaped clinical diagnosis in a considerable number of cases—from 26% to 42% in the several series cited. The percentage of cases not diagnosed must have been much higher in smaller rural places, where special diagnostic facilities were not available; and it is obvious that as these diagnostic facilities became available to a larger and larger proportion of the population, so the number of cases diagnosed must have steadily increased.

Mistakes in Pathological Diagnosis.—The mistakes in pathological diagnosis which were common in the early years of the century are much less frequent now; but they are not wholly extinct. Some pathologists still do not realize how easily secondary growths in the pleura, pericardium or cervical lymph glands may be mistaken for primary tumours. Of the 10 cases of "diffuse mesotheliomas" of the pleura reported by Godwin (1957), most of the descriptions are compatible with, and many of them strongly suggest, pulmonary carcinoma; and of 11 "primary tumours of the pleura" reported by McCaughey (1958), the descriptions and illustrations permit a fairly confident diagnosis of carcinoma of the lung in at least eight. Every year I receive for an opinion sections from supposedly primary pleural or other tumours which are almost certainly secondary to undiscovered, small primary carcinomas of the lung.

Concluding Comments on the Incidence of Carcinoma of the Lung.

From the foregoing outline the following main points emerge. In the later decades of last century, pathological records show that bronchial carcinoma was not a rare disease, although it was rarely identified as such by pathologists and was almost unknown to clinicians. In the first three decades of the present century, pathologists became increasingly aware of the characters of bronchial cancers, and the common "oat-cell" tumours were for the first time clearly recognized as carcinomas and not sarcomas. The fourfold increase in the number of lung-cancer death certificates which took place during this period is readily attributable to these advances in pathological knowledge. The last three decades have witnessed many further advances, not only in pathological knowledge, but also in the establishment of special chest clinics and thoracic surgery units with special diagnostic facilities and techniques—radiology, bronchoscopy and cytological and biopsy studies; and, even more important, clinicians as well as pathologists have become lung-cancer-conscious instead of lung-cancer-ignorant, as most of them were in the earlier period. Under these circumstances it was inevitable that increasing numbers of this clinically misleading and elusive disease should have been detected and correctly identified; and this progressive improvement in diagnosis certainly accounts for a large part of the greatly increased numbers of lung-cancer deaths registered during recent years. Whether or not improved diagnosis accounts for the whole of this increase we shall probably never know, for it is impossible to assess retrospectively just what proportion of clinical and pathological misdiagnoses were made at any given past time, and even now this proportion is still substantial, in spite of our greatly improved diagnostic armamentarium and our awareness of the disease.

It is pertinent to refer here to Doll's (1953) first two reasons for believing that there has been a real increase of lung cancer. His first reason was that "the increase in the recorded death rate still continues, despite the long period which has elapsed since attention was drawn to the importance of the disease". In my view the progressive improvement in diagnosis and the increasing awareness of the disease equally well account for this. Indeed, as Doll himself noted, there was already an indication in 1950 that the rising curve of the death rate might be commencing to flatten out to a plateau, for, while the male mortality figures between the ages of 35 and 44 years showed a steady rise from 1920 to 1946, the 1950 figure remained the same as it had been four years earlier. Perhaps in the near future the mortality rate for all ages will stabilize at a definite level; and, if it does, this may well mean that we have reached the limits of our diagnostic proficiency, rather than that the maximum effect of any particular carcinogen or set of carcinogens has been reached.

Doll's second reason for believing in a real increase was that "the disease is now so common that had the increase been entirely spurious it would be necessary to postulate that 50 years ago 95% of the fatal cases were wrongly certified". From my reading of the earlier, as well as the later, records (outlined in this lecture), and from my own experiences of lung cancer over four decades, I personally find no difficulty in postulating this. Let us recall (i) that at the beginning of the century this disease was regarded as rare, and yet that many cases of it, wrongly labelled, exist in earlier pathological records;

(ii) that, in the first three decades of this century, many pathologists had little knowledge of the disease, and pathological misdiagnosis was common; and (iii) that clinical awareness and diagnostic proficiency for lung cancer are largely products of the last three decades, and that even now, with all the special facilities available, something between 25% and 40% of cases still elude clinical detection. In the light of these facts, it is not improbable that 20 cases are correctly labelled now for every one correctly labelled 50 years ago.

Finally, let me add two disclaimers. The first is that I do not deny that there may have been a real increase of lung cancer. My conclusion is that it is not possible either to affirm or to deny this, for if such a real increase has occurred, it has been irretrievably lost to view in the far greater increase attributable to better knowledge and better diagnosis of this diagnostically elusive disease. My second disclaimer is that I do not consider that this indefinite conclusion about lung-cancer incidence throws any doubt on the ætiological role of smoking in lung cancer. The admirable studies of both the British and American workers on the comparative risks of lung cancer in smokers and non-smokers has proved beyond any shadow of doubt that smoking is an important cause of modern pulmonary cancer; and this conclusion would stand, whatever the trend of incidence of the disease, indeed, even if it was declining. The two problems are distinct and should not be confused. The validity of the statisticians' conclusions on the smoking-cancer relationship, revealed by *questionnaires*, needs no extraneous support from the argument of increasing incidence. Indeed, so controversial is the question of increased incidence that an attempt to link it with the incontrovertible evidence incriminating smoking as a cause weakens, not strengthens, the case against tobacco.

The Histological Variants of Pulmonary Carcinoma.

In my "Pathology of Tumours" (1948) I stressed that, while it is descriptively convenient to have names for the main structural variants of bronchial carcinoma—adenocarcinoma, squamous-cell carcinoma, oat-cell carcinoma, etc.—these names do not denote entities, and that there is only one entity, bronchial carcinoma, and great pleomorphism is possible in one tumour. In my own histological examination of 84 consecutive necropsy cases of pulmonary carcinoma at the Alfred Hospital, Melbourne, I found that about one-quarter of the tumours showed heterogeneous structure, and I realized that, as this estimate was based on only a few sections of each tumour, a more thorough and deliberate search would certainly have disclosed a higher proportion of tumours with diverse structure.

In recent years there have appeared a number of papers intended to show that the different histological types of bronchial carcinoma have different ætiologies, sex incidence and powers of metastasis. Most of these papers tacitly assume that the subdivision of pulmonary carcinoma into several histological types is a simple matter, not in need of discussion. My object here is to correct that false assumption, and to plead for a stricter use of names and more thorough examination of tumours, before coming to any far-reaching conclusions about the possible correlations of their histological structure with their causation and behaviour.

The Diverse Classifications of Different Pathologists.

The great diversity of the histological subdivisions adopted by different pathologists, and especially the widely differing percentages of tumours allotted to particular subgroups, are clear enough evidence of the real difficulty and arbitrary nature of subdivision. Walter and Pryce (1955) have given a useful comparison of some of the published series and have drawn special attention to the wide discrepancies in the numbers of tumours allocated to the various subgroups. Thus the proportion of tumours designated "adenocarcinoma" ranged from 4·9% to 39·4%, and of those designated "squamous-cell" from 6·9% to 75% in different series. Similarly, in a number of series reviewed by Mullaney (1958) the proportion of tumours designated "adenocarcinoma" ranged from 4·6% to 26%, and those designated "squamous-cell" from 28% to 62·9%. The idea that these differences may denote real differences in the incidence of the various histological types in different communities can be dismissed; not only is it inherently improbable, but similar discrepancies are found in the reports of different pathologists in one city. For example, Galuzzi and Payne (1955), examining the pathological records of cases of bronchial cancer from eight London hospitals, found wide differences in the proportions of non-squamous tumours which were designated "adenocarcinoma", ranging from 6% to 31%. From these and other figures it is clear, to quote Walter and Pryce, that "much of the variation is due to different interpretations by individual histologists", and that "even when the same terms are used by different pathologists, an identical tumour may be put into different categories". My own experience endorses this; I know of not a few cases in which a tumour showing both glandular and squamous differentiation has been called "adenocarcinoma" by one pathologist and "squamous-cell carcinoma" by another. Worse still, the compulsion to place a tumour of heterogeneous structure in one or another arbitrary category means that the same pathologist will classify the same tumour differently according to the piece he chances to examine.

How Frequent is Heterogeneous Structure?

As might be expected from the foregoing remarks, the proportion of tumours recorded as showing more than one structural variant differs greatly in different reported series. In many series, no indication of this is given, all tumours being arbitrarily allotted to one or another of three or more subgroups without discussion. In my Melbourne necropsy series, 19 out of 84 tumours (23%) showed heterogeneous structure. Subsequently, between 1948 and 1950, I examined 32 consecutive necropsy cases of pulmonary carcinoma at the Royal Cancer Hospital, London; 11 of these (34%) showed mixed structure—namely, combined anaplastic and squamous growth in six cases, anaplastic plus squamous plus adenocarcinoma in three cases, and combined anaplastic and adenocarcinoma in two cases. McGrath *et alii* (1952) found different structural variants in 45 of 87 carefully-studied tumours (52%); they interpreted this to mean that multiple tumour foci of different histological structure frequently coalesce, an interpretation which I am sure applies to only a small proportion of cases. Mullaney (1958), while placing his 100 tumours in four categories according to the predominant cell type, found more that one type of cell in 47 cases. Many other pathologists, though not giving numerical estimates, have stressed the frequency of heterogeneous structure in bronchial carcinoma. Bryson and Spencer (1951), while recognizing five histological types, stated that "two or more of the five types were often present together in the same tumour". Liebow (1952) wrote: "When very large sections or numerous blocks are studied, the incidence of mixed tumours is indeed high." Evans (1956) wrote: "A large number of bronchial carcinomata . . . show a marked degree of pleomorphism, so that any classification adopted must be arbitrary."

Comments on Particular Names for the Histological Variants.

"Oat-Cell" Carcinoma.—This is a frequent kind of structure, either alone or in combination with other structural variants. Several recent writers (for example, Walter and Pryce, 1955; Azzopardi, 1959) have held it to be a distinct entity, but my experience does not accord with this view. While there are many undifferentiated bronchial cancers which consist mainly or wholly of small elongated cells of nearly uniform size, there are many others in which this uniformity is lacking, and which show, along with "oat-cell" areas, large and pleomorphic cells, or glandular or squamous differentiation, or all of these. Barnard's classical paper in 1926 particularly stressed and depicted these variation, and his first conclusion reads: "In obvious carcinomata of the lung 'oat-

cells' have been found in addition to the more readily recognizable carcinoma cells. Similarly, in tumours composed for the most part of 'oat-cells' large polygonal cells and tubules lined by cubical or columnar cells have been seen."

Glandular differentiation is a frequent finding in predominantly undifferentiated, mainly "oat-cell", tumours; it was present in 12 of my 84 Australian necropsy cases and in five of my 32 London cases—that is, in 17 of 116 cases (15%). Although Walter and Pryce regarded "oat-cell" tumours as forming a distinct group, they found definite glandular differentiation in no less than 48% of these tumours, and in two tumours "differentiation was so extraordinarily well marked in places that they would be classified by most observers as adenocarcinomata". So also, Azzopardi (1959), though looking upon "oat-cell" carcinoma as "a special type of bronchial carcinoma which is sharply separable from squamous tumours and generally separable from adenocarcinoma", nevertheless found glandular differentiation, including mucin production, in 30 of 100 "oat-cell" tumours. But what is "adenocarcinoma" if it is not carcinoma with glandular differentiation? To the extent that an "oat-cell" tumour shows glandular differentiation, it is also, by definition, an adenocarcinoma. The view that "oat-cell" tumours are separable from "ordinary adenocarcinoma" (Walter and Pryce) depends on an arbitrary and personal idea as to what constitutes "ordinary adenocarcinoma".

Adenocarcinoma.—All pathologists will agree that this is the proper name for tumours which differentiate wholly or predominantly into acinar, tubular and papillary structures with or without mucin secretion. But, as we have just seen, there will be differences of opinion on the naming of "oat-cell" cancers with glandular differentiation. There will also be differences of opinion on how to name the so-called "malignant adenomas"—that is, those occasional members of the generally "benign" class of bronchial adenomas which prove themselves malignant by infiltrating widely or by metastasizing before they are treated. These tumours, both the benign and malignant ones, although clearly arising from the bronchial glands, often do not show any acinar differentiation, but consist of compact solid masses or trabeculæ of cells. Are we to call a malignant tumour of this kind an "adenocarcinoma", because, although it displays no glandular differentiation, we know its origin to have been glandular? Or is it preferable to place it in a separate class of "malignant adenomas"—or, better, "adenoma-like carcinomas"? A few members of this class have grown actively and to large sizes, and appear to have been frankly malignant *ab initio*; and in two of these which I have examined, in addition to adenoma-like growth, there has been more cellular diffuse growth approaching "oat-cell" carcinoma in appearance. McBurney *et alii* also saw atypical and pleomorphic structure in metastasizing "adenomas". Such tumours deserve thorough histological study, for they may help to clarify some of our ideas on the histogenesis and structural variations of bronchial cancer.

Squamous-Cell Carcinoma.—All pathologists will accept this name for tumours composed wholly of squamous stratified epithelium, though this may vary in its degree of differentiation and keratinization. But opinions and practice differ over the pigeon-holing of tumours containing much undifferentiated growth and relatively scanty squamous-cell foci, and over adenocarcinoma with areas of squamous cells. Thus, Walter and Pryce excluded from their squamous-cell group all tumours showing tubule formation; but they frequently found squamous metaplasia in their "adenocarcinomas", and in two cases "the primary tumour appeared to be squamous while the secondaries were mainly adenocarcinomatous. It is evident that squamous metaplasia may be so extensive that the parent type of growth is largely obscured". If this is true, and I am sure it is, then it is possible to argue that many or all squamous-cell carcinomas are basically adenocarcinomas with extensive squamous metaplasia. On the other hand, there is substantial evidence that some squamous-cell carcinomas take origin from bronchial mucosa which is already the seat of squamous metaplasia or of actual carcinoma-in-situ, especially in heavy smokers (Auerbach *et alii*, 1956 and 1957; Chang, 1957; Valentine, 1957). It remains for future studies to determine what proportion of predominantly squamous-cell growths develop in these two different ways. And, in the meantime, it will be wise to refrain from too rigid a separation of the supposedly "pure" squamous-cell tumours from the demonstrably adeno-squamous ones. We will return later to this important histogenetic point.

Histological Structure and Site.

Several workers have noted that predominantly squamous-cell growths more often arise from the large central bronchi than from the small peripheral ones, and that the converse applies to predominantly adenocarcinomatous tumours. Thus, Walter and Pryce (1955), studying surgically resected specimens, found the origin of 95 squamous-cell growths to be central in 55, peripheral in 35 and intermediate in 5; and while all of 27 adenocarcinomas were peripheral in origin, their 33 "oat-cell" carcinomas arose with equal frequency from central and peripheral bronchi. My own experience, mainly of necropsy cases, broadly accords with this generalization, except that I have seen many examples of adenocarcinomas which have unquestionably arisen from large bronchi, for example, the adenocarcinoma depicted in Figures 162 to 164 of my "Pathology of Tumours", arose from the left main bronchus, and the adenocarcinoma with diffuse spindle-cell growth which I reported in 1938 arose from the left upper lobe bronchus.

It is of some histogenetic interest that adenocarcinomas are relatively commoner at the periphery, where bronchial mucous glands are relatively few compared with the plentiful glands present in the larger bronchi. This suggests that not all adenocarcinomas necessarily arise from glands, but that some of them may arise from the surface epithelium. We know that the respiratory pseudostratified epithelium readily undergoes mucous glandular metaplasia in inflammatory and irritative states, and the same kind of metaplasia doubtless occurs in some of its tumours. Probably the glandular differentiation which is seen in "oat-cell" tumours is of this nature.

The fact that a high proportion of predominantly squamous-cell growths commence in large bronchi means that many of them will produce early respiratory symptoms, and so these patients will be more likely to be referred to chest clinics for special investigation. On the other hand, since many adenocarcinomas are peripheral, they are less likely to produce early respiratory symptoms, and more likely to produce a diversity of misleading clinical pictures by their metastases, and so more likely to be misdiagnosed. This difference is borne out by comparing the histological types of growth in surgical and necropsy series; as several workers (for example, Kreyberg, 1954) have noticed, surgical series usually contain a much higher proportion of squamous-cell growths and a lower proportion of adenocarcinomas than necropsy series.

Histological Structure and Sex.

Many workers have noticed that adenocarcinomas are relatively frequent and squamous-cell carcinomas relatively infrequent in women; but here also estimates have differed widely, as is shown in Table I. For comparison I have included in this my own Melbourne and London cases, the percentages in parentheses denoting all tumours showing glandular or squamous differentiation respectively, those showing both (9% of male cases and 5% of female cases) thus appearing in both categories. The proportion of tumours designated adenocarcinomas thus ranged from 3% to 31% in males, and from 13% to 67% in females—a significant difference; and the proportion designated squamous-celled ranged from 19% to 60% in males, and from 7% to 16% in females—again a significant difference.

Histological Structure and Metastasis.

Many workers have noted that, in general, predominantly squamous-cell growths metastasize less

frequently and less widely than either predominantly adenocarcinomatous or undifferentiated ones (for example, Bryson and Spencer, 1951; Galluzzi and Payne, 1955 and 1956; Strauss and Weller, 1957). This difference is not very surprising, since we know that well-differentiated squamous-cell carcinomas of any site are, in general, less productive of metastases than undifferentiated ones, or those showing adenocarcinomatous structure.

TABLE I.

Percentages of Squamous-Cell Carcinoma and Adenocarcinoma in Males and Females in Different Reported Series.[1]

Series.	Males.		Females.	
	Adeno-carcinoma.	Squamous-Cell Carcinoma.	Adeno-carcinoma.	Squamous-Cell Carcinoma.
Bryson and Spencer (1951), 866 autopsy cases (London) ..	3	19	13	14
Kreyberg (1954), 193 clinical cases (Norway)	6	60	60	10
Galluzzi and Payne (1955), 741 autopsy cases (London) ..	12	27	17	15
Strauss and Weller (1957), 296 autopsy cases (U.S.A.) ..	31	41	67	7
Willis, 116 autopsy cases (Melbourne and London) ..	16 (25)	28 (37)	42 (47)	11 (16)

[1] For Galluzzi and Payne's series percentages are estimated as nearly as possible from their graph. The figures in parentheses in my own series denote percentages calculated when tumours showing both glandular and squamous differentiation are included—figures which none of the other series gives.

Histological Structure and Causation.

Kreyberg's conclusions from his Norwegian findings (1952, 1954 and 1955), endorsed by Doll, Hill and Kreyberg (1957) on some British material, cannot be better summarized than in the opening words of their paper, which I therefore quote:

> The histological types of lung cancer . . . can be divided into two ætiologically distinct groups. The squamous cell, large cell and small cell carcinomas (including oat-cell carcinomas) form the first group. These types . . . might be histological variants of a single oncological entity and be produced largely by exposure to an external factor (or factors) which have recently increased in prevalence and to which men are principally exposed. The second group is heterogeneous and consists of adenocarcinomas, bronchiolar (alveolar cell) carcinomas and various grades of adenoma [which may be attributed to] different ætiological factors . . . of approximately constant prevalence to which men and women are exposed equally.

Because these conclusions are so important and far-reaching, it is all the more essential that the foundations on which they are based should be critically examined. The following points must be noted:

1. There is no indication in any of Kreyberg's papers of the adequacy or otherwise of the material on which his histological subdivisions were made. It comprised two clinical series and two necropsy series of cases, but we are not told anything of the extent or technique of examination of any of these—whether some of them were only biopsies, how many and how large were the sections from whole lungs, and whether or not metastases in necropsy cases were examined microscopically. As we have seen, information on these matters is essential if we are to judge the reliability of any worker's arbitrary histological subdivisions.

2. In his 1952 paper, Kreyberg noted that four of his first 100, mainly surgical, specimens showed mixed squamous and glandular structure; but his later papers, in which he makes a sharp separation between squamous-cell and glandular tumours, ignores this important mixed group. Moreover, there is clear evidence that the size of this group is larger than the 4% mentioned in Kreyberg's first paper; for example, I found both kinds of differentiation in nine of 136 necropsy cases (7%), Walter and Pryce found squamous change in 19% of their surgical and 12% of their necropsy adenocarcinomas, and Phillips *et alii*, using a whole section technique, found squamous changes in all of nine adenocarcinomas.

3. Kreyberg's grouping together of squamous-cell growths and undifferentiated, mainly "oat-cell", growths as an "oncological entity" distinct from adenocarcinoma is histologically unwarranted. As we have seen, glandular differentiation is common in "oat-cell" tumours—commoner than squamous-cell differentiation; it was present in 48% of Walter and Pryce's "oat-cell" tumours and in 30% of Azzopardi's. On histological evidence, then, there is more reason to suppose "oat-cell" tumours to be akin to adenocarcinomas than to squamous-cell carcinomas.

4. On histogenetic principles also there are objections to the sharp separation of squamous-cell carcinoma and adenocarcinoma. Since all bronchial cancers arise from epithelia which are normally non-squamous, any squamous characters in the tumours must be attributed to metaplasia—squamous metaplasia either in the epithelia before the development of the tumours or in the tumours themselves. While there are grounds for believing that some tumours may arise in mucosa which is already the seat of metaplasia (McGrath *et alii*, 1952; Auerbach *et alii*; Chang, 1957; Valentine, 1957), there is clear structural evidence that in a great many cases squamous change takes place in the tumours themselves. This applies to the mixed adeno-squamous tumours, which Kreyberg omits, but which, as we have seen, form a considerable proportion of lung cancers. Squamous metaplasia in tumours that are basically adenocarcinomas is not peculiar to the lung; it is well known in adenocarcinomas of many other parts, notably those of the endometrium, gall-bladder and gastro-intestinal tract. It would, therefore, be very surprising if this general principle did not apply to bronchial tumours—which would be the case if, as Kreyberg holds, adenocarcinomas and squamous-cell carcinomas were distinct entities.

Finally, I would question the validity of one of Kreyberg's statistical conclusions (1954). In Norway, during the twenty-year period from 1930 to 1950, the number of registered deaths attributed to lung cancer rose four and a half times for women and seven times for men. Because in his clinical and necropsy material he had found an increasing proportion of his Group I tumours (squamous-cell and undifferentiated carcinomas) in men, while "in females the ratio of the different tumour types has not changed appreciably", Kreyberg concluded that the four and a half times increase of registered female deaths was an "indicator of the increased diagnostic efficiency", and that "the difference between this figure and the seven-fold increase registered in males is taken to represent the real increase in the development of lung cancer in males". But if a four and a half times increase was due to better diagnosis, why not a seven times one? The latter is less than double the former; and this moderate difference, and also the difference in histology in the mounting male series, may have been due partly to the fact that predominantly squamous-cell cancers, which are commoner in males, are more productive of symptoms and therefore bring the patients more often to the special chest clinics for investigation, and partly to Kreyberg's neglect of the important group of adeno-squamous tumours, the fortuitous and arbitrary misplacing of some of which in one or another of his two great composite groups might easily have influenced his ratios.

In conclusion, I do not deny the possibility that there may have been some real increase in lung cancer in Norway in recent years, or that this increase may have been in males only, or that it may have been accompanied by a change in the histological spectrum of the tumours; but in my view the evidence for none of these propositions is conclusive, and more thorough examination of both surgical and necropsy material, with a more critical appraisal of the structural versatility of bronchial cancer, is essential before any conclusions on these questions are drawn.

Summary.

Lung cancer was not an uncommon disease in the later decades of the last century, but pathologists' knowledge of it was very imperfect, and most of them regarded it erroneously as a rare disease until the late 1930's. Its adequate clinical diagnosis came later still, with the increase of special chest clinics with special diagnostic facilities; and even today, with all these facilities, a considerable number of cases of the disease still escapes detection in large metropolitan hospitals.

A large part of the great increase in registered deaths from lung cancer which has occurred in this century is certainly due to better diagnosis and to a greater clinical awareness of the disease. Whether or not there has also been a real increase in its frequency, it is impossible to be sure. The incrimination of smoking as a cause of lung cancer is clear and certain, without reliance on the dubiously valid proposition that the disease has recently increased in frequency.

In histological structure pulmonary carcinoma is highly pleomorphic, and its subdivision into histological types is highly arbitrary. While some rough correlations can be descried between histological structure on the one hand and site, sex incidence and metastatic behaviour on the other, there are many exceptions to all the rules. On the possible correlation of histological structure with ætiology, it is premature to come to any conclusions; more thorough structural studies with critical appraisal of the terms used are necessary.

References.

AUERBACH, O., *et alii* (1956), "Anatomical Approach to Study of Smoking and Bronchogenic Carcinoma; Preliminary Report of 41 Cases", *Cancer (Philad.)*, 9: 76.

AUERBACH, O., *et alii* (1957), "Changes in the Bronchial Epithelium in Relation to Smoking and Cancer of the Lung; a Report of Progress", *New Engl. J. Med.*, 256: 97.

AZZOPARDI, J. G. (1959), "Oat-Cell Carcinoma of the Bronchus", *J. Path. Bact.*, 78: 513.

BARNARD, W. G. (1926), "The Nature of the 'Oat-celled Sarcoma' of the Mediastinum", *J. Path. Bact.*, 29: 241.

BONSER, G. M. (1928), "Incidence of Tumours of Respiratory Tract in Leeds", *J. Hyg. (Lond.)*, 28: 340.

BONSER, G. M. (1934), "Incidence of Intrathoracic Tumours in Leeds", *J. Hyg. (Lond.)*, 34: 218.

BONSER, G. M. (1938), "Incidence of Intrathoracic Cancer in Great Britain, with Special Reference to Leeds", *Acta Un. int. Cancr*, 3: 119.

BRYSON, C. C., and SPENCER, H. (1951), "Carcinoma of Bronchus; Clinical and Pathological Survey of 866 Cases", *Quart. J. Med.*, 44: 173.

CHANG, S. C. (1957), "Microscopic Properties of Whole Mounts and Sections of Human Bronchial Epithelium of Smokers and Nonsmokers", *Cancer (Philad.)*, 10: 1246.

COATS, J. (1888), "Case of Multiple Cancerous Tumours, Many of Them Cystic, in the Lungs, Brain, Bones, etc.; the Primary Tumour Probably in the Lung", *Trans. Path. Soc. Lond.*, 39: 326.

DAFF, M. E., DOLL, R., and KENNAWAY, E. L. (1951), "Cancer of Lung in Relation to Tobacco", *Brit. J. Cancer*, 5: 1.

DOLL, R. (1953), "Bronchial Carcinoma; Incidence and Ætiology", *Brit. med. J.*, 2: 521.

DOLL, R., HILL, A. B., and KREYBERG, L. (1957), "The Significance of Cell Type in Relation to Ætiology of Lung Cancer", *Brit. J. Cancer*, 11: 43.

DRURY, R. A. B., and STIRLAND, R. M. (1959), "Carcino-Sarcomatous Tumours of the Respiratory Tract", *J. path. Bact.*, 77: 543.

ELLMAN, P., HENSON, R. A., and SELLORS, T. H. (1953), "Discussion: Unusual Manifestations of Bronchial Carcinoma", *Proc. roy. Soc. Med.*, 46: 851.

EVANS, R. W. (1956), "Histological Appearances of Tumours", Livingstone, Edinburgh and London.

FRIED, B. M., and BUCKLEY, R. C. (1930), "Primary Carcinoma of Lungs; Intracranial Metastases", *Arch. Path. (Chicago)*, 9: 483.

FULLERTON, J. M. (1956), "Carcinoma of the Lung", *Brit. med. J.*, 1: 1238.

GALLUZZI, S., and PAYNE, P. M. (1955), "Bronchial Carcinoma; Statistical Study of 741 Necropsies with Special Reference to Distribution of Blood-borne Metastases", *Brit. J. Cancer*, 9: 511.

GALLUZZI, S., and PAYNE, P. M. (1956), "Brain Metastases from Primary Bronchial Carcinoma: A Statistical Study of 741 Necropsies", *Brit. J. Cancer*, 10: 408.

GODWIN, M. C. (1957), "Diffuse Mesotheliomas, with Comment on their Relation to Localized Fibrous Mesotheliomas", *Cancer (Philad.)*, 10: 298.

HANDFORD, H. (1888), "Two Cases of Mediastinal Cancer", *Trans. path. Soc. Lond.*, 39: 48.

HANDFORD, H. (1890), "Carcinoma of Root of Lung", *Trans. path. Soc. Lond.*, 41: 37.

HEADY, J. A., and KENNAWAY, E. L. (1949), "Increase in Deaths Attributed to Cancer of Lung", *Brit. J. Cancer*, 3: 311.

KARSNER, H. T., and SAPHIR, O. (1930), "Small Cell Carcinomas of Lung", *Amer. J. Path.*, 6: 553.

KENNAWAY, E. L., and KENNAWAY, N. M. (1947), "Further Study of Incidence of Cancer of Lung and Larynx", *Brit. J. Cancer*, 1: 260.

KENNAWAY, N. M., and KENNAWAY, E. L. (1936), "Study of Incidence of Cancer of Lung and Larynx", *J. Hyg. (Lond.)*, 36: 236.

KREYBERG, L. (1952), "One Hundred Consecutive Primary Epithelial Lung Tumours", *Brit. J. Cancer*, 6: 112.

KREYBERG, L. (1954*a*), "Significance of Histological Typing in Study of Epidemiology of Primary Epithelial Lung Tumours", *Brit. J. Cancer*, 8: 199.

KREYBERG, L. (1954*b*), "Occurrence of Lung Cancer in Norway", *Brit. J. Cancer*, 8: 209.

KREYBERG, L. (1954*c*), "Geographical Distribution of Histological Sub-groups of Primary Epithelial Lung Tumours in Norway", *Brit. J. Cancer*, 8: 599.

KREYBERG, L. (1955), "Lung Cancer and Tobacco Smoking in Norway", *Brit. J. Cancer*, 9: 495.

MACCALLUM, W. G. (1940), "A Textbook of Pathology", Saunders, Philadelphia.

MCBURNEY, R. P., KIRKLIN, J. W., and WOOLNER, L. B. (1953), "Metastasizing Bronchial Adenomas", *Surg. Gynec. Obstet.*, 96: 482.

MCCAUGHEY, W. T. E. (1958), "Primary Tumours of the Pleura", *J. Path. Bact.*, 76: 517.

MCGRATH, E. J., GALL, E. A., and KESSLER, D. P. (1952), "Bronchiogenic Carcinoma, Product of Multiple Sites of Origin", *J. thorac. Surg.*, 24: 271.

MOORE, N. (1884), "Endothelioma of Mediastinum", *Trans. path. Soc. Lond.*, 35: 272.

MULLANEY, P. J. (1958), "A Survey of 100 Consecutive Malignant Epithelial Lung Tumours", *Brit. J. Cancer*, 12: 327.

NASH, A. D., and STOUT, A. P. (1958), "Giant Cell Carcinoma of the Lung; Report of Five Cases", *Cancer (Philad.)*, 11: 369.

PASSEY, R. D., and HOLMES, J. M. (1935), "Incidence of Intrathoracic Neoplasia in Teaching Hospitals of Great Britain", *Quart. J. Med.*, 28: 321.

PHILLIPS, F. J., BASSINGER, C. E., and ADAMS, W. E. (1950), "Bronchiogenic Carcinoma; Pathologic Clinical Correlative Study of Full-Size Mounts from Operated Carcinomas", *J. thoracic. Surg.*, 19: 680.

PITT, G. N. (1888), "Malignant Disease of Bronchial Glands" and "Primary Cancer of Pleura", *Trans. path. Soc. Lond.*, 39: 54 and 56.

REGISTRAR-GENERAL'S STATISTICAL REVIEW OF ENGLAND AND WALES (1956), Commentary: 186 and 191.

SIMPSON, S. L. (1929), "Primary Carcinoma of the Lung", *Quart. J. Med.*, 22: 413.

SITSEN, A. E. (1935), *"Wird der Lungenkrebs häufiger? (Eine kritisch-statistische Erörterung)"*, *Z. Krebsforsch.*, 42: 30.

STEINER, P. E. (1944), "Incidence of Primary Carcinoma of Lung with Special Reference to its Increase", *Arch. Path. (Chicago)*, 37: 185.

STRAUSS, B., and WELLER, C. V. (1957), "Bronchogenic Carcinoma; a Statistical Analysis of 296 Cases with Necropsy as to Relationships between Cell Types, Age, Sex and Metastasis", *Arch. Path. (Chicago)*, 63: 602.

TEIR, H., and KOIVUNIEMI, A. (1959), "Post-mortem Observations on Clinical Tumour Diagnoses", *Ann. Med. intern. Fenn.*, 48: 296.

TURNER, F. C. (1888) "A Case of Cystic Growths in the Cerebellum and Right Adrenal", *Trans. path. Soc. Lond.*, 39: 9.

VALENTINE, E. H. (1957), "Squamous Metaplasia of the Bronchus: A Study of Metaplastic Changes Occurring in the Epithelium of the Major Bronchi in Cancerous and Non-cancerous Cases", *Cancer (Philad.)*, 10: 272.

WALTER, J. B., and PRYCE, D. M. (1955), "Histology of Lung Cancer", *Thorax*, 10: 107.

WALTER, J. B., and PRYCE, D. M. (1955), "Site of Origin of Lung Cancer and its Relation to Histological Type", *Thorax*, 10: 117.

WILLIS, R. A. (1938), "Metastatic Deposit of Bronchial Carcinoma in Hydrocele Misdiagnosed 'Endothelioma', with Review of Supposed Endotheliomas of Serous Membranes", *J. Path. Bact.*, 47: 35.

WILLIS, R. A. (1948), "Pathology of Tumours", Butterworth, London.

NEW NAMES IN TUMOUR TERMINOLOGY.[1]

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THE following assessment of the merits or demerits of some recently introduced tumour names is necessarily summary and kaleidoscopic; for fuller discussion, reference may be made to Willis (1959 and 1960).

Myo-epithelioma.

Myo-epithelial differentiation undoubtedly takes place in many sweat-gland and apocrine tumours (Mayer, 1941; Sheldon, 1941; Hartz, 1946; Nangle and Symmers, 1950). Recent studies have also brought good evidence that the frayed-out meshworks and filaments of cells in mucoid areas of salivary tumours are of myo-epithelial nature (Sheldon, 1943; Bauer and Fox, 1945; Bauer and Bauer, 1953), and that they produce a mucin different from that of the secreting epithelial cells and more resembling a connective-tissue mucin (Azzopardi and Smith, 1959). However, it is doubtful whether tumours in which myo-epithelial tissue is abundant merit the special name "myo-epithelioma", since they are only variants of classes for which we already have more than enough names.

Muco-epidermoid Carcinoma.

The name "muco-epidermoid carcinoma" was applied by Stewart *et alii* (1945) to a group of salivary tumours showing mingled squamous-cell and mucous-cell characters. Since these growths seldom show other structural variations of kinds commonly seen in the pleomorphic salivary tumours, and since they behave more malignantly than most of the pleomorphic class, they merit a distinguishing name; but this does not mean that they are histogenetically a distinct species. Extension of the name "muco-epidermoid" to tumours of skin, bronchi or other organs is unwise.

Acinic-Cell Adenocarcinoma.

The name "acinic-cell adenocarcinoma" also, introduced by Godwin *et alii* (1954), is a useful one for distinguishing salivary tumours composed mainly or wholly of basophilic-granular cells or clear cells, arranged in acinar, papillary or solid formations, and evidently representing the secreting acinar cells.

Cylindroma.

The antique name "cylindroma" was coined over 100 years ago by Billroth to describe an orbital tumour, possibly of nasal origin, composed of columns of cells surrounded by cylindrical sheaths of hyaline collagen. It was soon found that tumours of similar structure occurred in the salivary glands, and the name was applied to these also. Great controversy ensued as to their histogenesis, the favourite view being that they were endotheliomas or peritheliomas, an idea seriously considered as late as 1936 (MacCallum). It is regrettable that the histogenetically meaningless nickname "cylindroma" has recently again become popular for certain tumours of the skin, of the salivary or other oral glands, of the nasal cavity, of the lachrymal glands, and of the tracheal and bronchial glands. It would be far better to call these tumours cribriform or adenoid cystic carcinomas.

Olfactory Esthesioneuroepithelioma.

This cumbersome but correct name was first introduced by Berger *et alii* (1924), and used by Berger and Coutard (1926) to denote a distinctive class of rare malignant tumours which arise from the olfactory sensory mucosa in adults. Useful recent accounts are by Mendeloff (1957) and Aldave and Gallager (1959).

Retinal Anlage Tumour.

This name, first applied by Halpert and Patzer (1947) to the rare pigmented growths of the jaws of infants, was widely, but uncritically, accepted. Elsewhere (1958) I have given the reasons for rejecting this name and for concluding that the growth arises from the paradental epithelial residues, as indeed was clearly shown by Mummery and Pitts in their account of the first reported case in 1926.

Hibernoma.

This name was applied to the tumour of brown fat, because this kind of fat is conspicuous in the so-called "hibernating glands" of rodents. The name "hibernoma", like the name "hibernating gland", is a poor one, but it has persisted because it is simpler than the phrase "brown-fat lipoma". The best recent review is that of R. W. Cox of Auckland, New Zealand (1954).

Myelolipoma.

This name has been applied particularly to masses of heterotopic fatty and hæmatopoietic marrow which develop in the adrenal gland, usually in middle-aged or old people (Collins, 1932; De Navasquez, 1935; Giffen, 1947; Holliday, 1955; McDonnell, 1956; Plaut, 1958). The marrow tissue, although well circumscribed, is not encapsulated, but mingles with the zone of cortical tissue which surrounds it. The cause is unknown; the patients have not had any special blood diseases, and the adrenal lesions have been only incidental necropsy findings. It is doubtful whether they are true tumours, although some of them have attained a large size—for example, 8 cm. in diameter and 245 grammes in weight in De Navasquez's case. Very rarely large lipomas in other parts of the body—for example in retroperitoneal or intrathoracic situations—are found to contain small or large areas of hæmatopoietic tissue with all the elements of bone marrow, meriting the name myelolipoma (Blaisdell, 1933; Dodge and Evans, 1956; Foster, 1958).

Thymolipoma.

A few cases have been reported of large fatty tumours of the thymus, usually in adults, with plentiful persistent thymic tissue scattered through the fatty tissue (Hall, 1949; Dunn and Frkovich, 1956; Unver, 1957). One such tumour, shown to me by Dr. A. J. Shillitoe of Hull, was removed surgically from a boy aged seven years; it weighed 154 grammes and contained a great quantity of normal-looking thymic tissue, suggesting that either a greatly hyperplastic thymus, or possibly a highly differentiated thymoma, was undergoing adipose replacement. This interesting group of tumours needs further study.

Mesenchymoma.

This name has been applied to connective-tissue tumours which occur in adults, usually in the limbs or parietes, and which are usually malignant, with two or more varieties of tissue discernible—fibroblastic, mucoid, adipose, hæmatopoietic, osteoid or cartilaginous (Gilmour, 1943; Symmers and Nangle, 1951; Sevitt, 1956). However, by other workers the name has also been used to embrace a variety of other and unrelated tumours—for example, the mixed tumours of the breast, endometrium and urinary organs, and even the granulosa-cell and theca-cell tumours of the ovary (Novak, 1947). Thus the name has lost precision and has become confusing. It is also open to objection in that it may be wrongly taken to imply an origin from embryonic mesenchyme, whereas the tumours in question arise in adults and are unrelated to the truly embryonic sarcomas of childhood. However, provided that we are not misled in this way and that we use it in its restricted sense, "mesenchymoma" is a useful nickname for adult connective-tissue tumours which display diverse lines of differentiation. It serves to remind us of the plasticity or metaplastic potentialities of neoplastic mesenchymal tissues.

Hæmangiopericytoma.

This name was introduced by Stout (Stout and Murray, 1942; Stout, 1949 and 1956) to denote a group of rare tumours arising from the pericytes of Zimmermann, and thus akin to glomangiomas, but less highly organized,

[1] Read at the Cancer Congress of the Anti-Cancer Council of Victoria on August 24, 1960, at Melbourne.

consisting of masses of plump polyhedral or fusiform cells packed between the channels of a rich vascular plexus. The tumours occur in the limbs, retroperitoneum, mediastinum and viscera, usually in adults; they may grow to a large size, and are usually well-defined and benign, but occasionally they are malignant. There is, I think, no doubt that an entity properly designated hæmangiopericytoma does indeed exist; I have seen several acceptable benign examples. But the utmost caution is needed in applying the name to atypical and malignant growths, since other kinds of tumours, especially carcinomas, can simulate the structure regarded as characteristic of hæmangiopericytoma. I know of more than one case in which this diagnosis was made confidently by several experienced pathologists, and the growth was subsequently shown to be carcinomatous. We must guard against the mistake of making this name a dumping ground for obscure tumours of other kinds, as has happened in the past with the name "endothelioma".

Recent Names for Tumours and Pseudo-Tumours of Bone.

In recent years Jaffe (1958) and Lichtenstein (1952) have done useful service in segregating from the sundry "odd" tumours or tumour-like lesions of bone several groups on which they have focused attention by the introduction of special names. These are briefly as follows.

Osteoid Osteoma.

This is the name given to a centrally-situated, benign, circumscribed, painful lesion in a young person, often only 1 cm. or less in diameter, composed of vascular osteoid tissue and new bone. Many pathologists doubt that it is a tumour and regard it instead as an ossifying variant of fibrous dysplasia.

Benign Osteoblastoma.

This is the name applied to lesions akin to osteoid osteoma, but larger, less densely ossified and less painful (Lichtenstein, 1956). Such lesions may be mistaken histologically for osteosarcoma.

Benign Chondroblastoma.

This is the name preferred by Jaffe and Lichtenstein for Codman's "chondromatous giant-cell tumor", a circumscribed, benign lesion of a long bone, especially the upper end of the humerus, in a young person, seen microscopically to be an intimate mixture of cartilaginous and osteoclastic tissue.

Chondromyxoid Fibroma.

This is Jaffe and Lichtenstein's name for benign, circumscribed lesions composed mainly of connective tissue, which, although not frankly cartilaginous, have "chondroid and myxoid traits". Dahlin (1956), in a careful study of 11 specimens, concluded that "chondromyxoid fibroma is closely related to benign chondroblastoma", since many lesions showed the structure of both. My own experience accords with this, and I think it is a mistake to distinguish them by special names, especially as the merits of the names themselves are questionable on other grounds. Recently Lichtenstein himself (Lichtenstein and Bernstein, 1959) has reported seven "atypical benign chondroblastomas" and seven "atypical chondromyxoid fibromas", and has admitted that "there is a gamut of peculiar tumours of bone, which . . . may be designated as chondroid".

In my opinion it is probable that most of the lesions which have been designated by the names just discussed are not tumours at all but variants of fibrous dysplasia—osteoid osteoma and benign osteoblastoma its ossifying variants, and benign chondroblastoma and chondromyxoid fibroma its chondrifying variants.

Granular-Cell Myoblastoma.

In the first edition of my "Pathology of Tumours" (1948) I objected to the then-popular name "granular-cell myoblastoma", on the grounds that it was being applied uncritically to a number of different lesions, many of them unrelated to skeletal muscle, and that the lingual lesions and others involving muscle are almost certainly not neoplastic. These objections have since been vindicated, and several different classes of lesions which were formerly called myoblastomas have been identified and separated. These include: (i) the granular-cell epulides of infants, which are probably derived from the paradental residues (Willis, 1958); (ii) the tumours of the glomus jugulare, which are now clearly recognized as chemodectomas akin to those of the carotid body (see below); and (iii) the peculiar and distinctive alveolar granular-cell tumour of the thigh or other parts, which also may be a chemodectoma (see below). It is probable that, with further study, more and more of the granular-cell growths formerly dumped together as myoblastomas will be correctly identified as other things, until the dump will have disappeared and this bad name will have become completely obsolete.

Chemodectoma.

This is a useful generic name, briefer than the alternative "non-chromaffin paraganglioma", for the tumours of the various chemoreceptor organs—namely, the carotid body, the aortic and pulmonary bodies, the glomus jugulare, the ganglion nodosum and other glomera of the vagus nerve, and microscopic unnamed glomera which are probably present in the retroperitoneum, thigh and other parts. Elsewhere (Willis, 1959) I have given a brief review of reported tumours of these various glomera.

Special comment is called for on the group of not very rare tumours of the thigh and other parts in young people, which were formerly called "myoblastomas", but which Smetana and Scott (1951) distinguished as "malignant tumors of non-chromaffin paraganglia" and Christopherson *et alii* (1952) as "alveolar soft-part sarcomas". Clinically, as well as histologically, these tumours form a distinctive class; but their exact histogenesis is still uncertain, and further work is needed to identify their source. It is quite likely, I think, that this will prove to be special chemoreceptors, as Smetana and Scott first suggested. Among recent reports is a good account of three cases by Hurley (1956) from the Department of Pathology, University of Melbourne.

Arrhenoblastoma and Kindred Names.

The name "arrhenoblastoma" was invented by Meyer for maculinizing tumours of the ovary. It is an unfortunate one, since there is no such cell as an "arrhenoblast", and the implication that the tumours must arise from male elements in the ovary is erroneous. It now seems clear that androgen-producing tumours of the ovary can arise from several different sources, some being essentially granulosa-cell or theca-cell tumours which have assumed perverted androgenic instead of œstrogenic activity, others being hilar-cell tumours and still others containing both hilar cells and follicular elements, while very rarely an adrenal cortical tumour arises from a juxta-ovarian nodule of adrenal cortex.

The name "gynandroblastoma" has been applied to ovarian tumours in patients with masculinization who continued to menstruate and showed other signs of hyperœstrinism (Mechler and Black, 1943); but it is histologically meaningless and of doubtful value. Even more objectionable is the word "masculinovoblastoma" for lipoid-rich masculinizing tumours of the ovary (Rottino and McGrath, 1939; Merivale and Forman, 1951); and Lees and Paine (1958), in describing a striking tumour of this kind, wisely avoided this histogenetically absurd word. Hilar-cell tumours, like their testicular counterparts, often show lipoid-rich cells; and most of the "masculinovoblastomas" which have been reported have almost certainly been hilar-cell tumours.

Dysgerminoma.

This is Meyer's name for seminoma-like tumours of the ovary; but their histogenesis is still unsettled, and there

is need of further hormonal and histological studies of cases, including nuclear sexing. Hermaphroditism or pseudohermaphroditism is present in a considerable number of cases, and it may well be found that some of the tumours indeed arise from testicular tissue in genetic males (see Carpentier *et alii*, 1956). Hughesdon (1959) on the other hand, in a searching discussion of the histogenesis of "dysgerminoma", gives evidence that it may be oocytic (or rather oogonial) in nature.

Mesonephroma.

This is Schiller's (1939) name for certain cystic ovarian tumours; it is based on a supposed resemblance of their elements to "glomeruli" and "abortive renal tubules". While many later writers have accepted this kind of a tumour as an entity, they have disputed its mesonephric origin, and several other equally speculative ideas about its histogenesis have been advanced—for example, that it is a "papillo-endothelioma" (Kazanicigil *et alii*, 1940), a "teratoid adenocystoma" (Stromme and Traut, 1943), an "extraembryonic mesoblastoma of germ cell origin" (Teilum, 1950) or "an extraembryonic yolk sac-allantoic tumor or an endodermal sinus tumor" (Teilum, 1959). This last suggestion, based solely on a histological resemblance of parts of the tumour to the allantoic and yolk-sac elements in the rat's placenta, illustrates the fantastic lengths to which a flight of pathological imagination may be carried.

References.

ALDAVE, A., and GALLAGER, H. S. (1959), "Olfactory Esthesioneuroepithelioma", *A.M.A. Arch. Path.*, 67: 43.

AZZOPARDI, J. G., and SMITH, O. D. (1959), "Salivary Gland Tumours and Their Mucins", *J. Path. Bact.*, 77: 131.

BAUER, W. H., and BAUER, J. D. (1953), "Classification of Glandular Tumours of Salivary Glands; Study of 143 Cases", *A.M.A. Arch. Path.*, 55: 328.

BAUER, W. H., and FOX, R. A. (1945), "Adenomyoepithelioma (Cylindroma) of Palatal Mucous Glands", *A.M.A. Arch. Path.*, 39: 96.

BERGER, L., and COUTARD, H. (1926), *"L'esthésioneurocytome olfactif", Bull. Ass. franç. Cancer*, 15: 404.

BERGER, L., LUC, —, and RICHARD (1924), *"L'esthésioneurocytoma olfactif", Bull. Ass. franç. Cancer*, 13: 410.

BLAISDELL, J. L. (1933), "Extramedullary Hæmatopoiesis in Retroperitoneal Tumor", *A.M.A. Arch. Path.*, 16: 643.

CARPENTIER, P. J., STOLTE, L. A. M., and VISSCHERS, G. P. (1956), "Gonadal Dysgenesis and Testicular Tumours", *Lancet*, 1: 386.

CHRISTOPHERSON, W. M., FOOTE, F. W., and STEWART, F. W. (1952), "Alveolar Soft-Part Sarcomas; Structurally-Characteristic Tumors of Uncertain Histogenesis", *Cancer (Philad.)*, 5: 100.

COLLINS, D. C. (1932), "Formation of Bone Marrow in Suprarenal Gland", *Amer. J. Path.*, 8: 97.

COX, R. W. (1954), "'Hibernoma'; Lipoma of Immature Adipose Tissue", *J. Path. Bact.*, 68: 511.

DAHLIN, D. C. (1956), "Chondromyxoid Fibroma of Bone, with Emphasis on its Morphological Relationship to Benign Chondroblastoma", *Cancer (Philad.)*, 9: 195.

DE NAVASQUEZ, S. (1935), "Case of Myelo-Lipoma (Bone Marrow Heterotopia) of Suprarenal Gland", *Guy's Hosp. Rep.*, 85: 237.

DODGE, O. G., and EVANS, D. M. D. (1956), "Hæmopoiesis in Presacral Fatty Tumour (Myelolipoma)", *J. Path. Bact.*, 72: 313.

DUNN, B. H., and FRKOVICH, G. (1956), "Lipomas of Thymus Gland with Illustrative Case Report", *Amer. J. Path.*, 32: 41.

FOSTER, J. B. T. (1958), "Primary Thoracic Myelolipoma; Case Report", *A.M.A. Arch. Path.*, 65: 295.

GIFFEN, H. K. (1947), "Myelolipoma of Adrenals; Report of Seven Cases", *Amer. J. Path.*, 23: 613.

GILMOUR, J. R. (1943), "A Recurrent Tumour of Mesenchyme in an Adult", *J. Path. Bact.*, 55: 495.

GODWIN, J. T., FOOTE, F. W., and FRAZELL, E. L. (1954), "Acinic-Cell Adenocarcinoma of Parotid Gland; Report of 27 Cases", *Amer. J. Path.*, 30: 465.

HALL, G. F. M. (1949), "Case of Thymolipoma; with Observations on Possible Relationship to Intrathoracic Lipomata", *Brit. J. Surg.*, 36: 321.

HALPERT, B., and PATZER, R. (1947), "Maxillary Tumors of Retinal Anlage", *Surgery*, 22: 837.

HARTZ, P. H. (1946), "Adenomyoepithelioma of Sweat Gland; Report of Cases", *Amer. J. Clin. Path.*, 16: 385.

HOLLIDAY, T. D. S. (1955), Massive Bone-Marrow Heterotopia in Both Adrenal Glands", *J. Path. Bact.*, 70: 239.

HURLEY, J. V. (1956), "Alveolar Soft-Part Sarcoma", *Aust. N.Z. J. Surg.*, 26: 122.

JAFFE, H. L. (1958), "Tumors and Tumorous Conditions of the Bones and Joints", Henry Kimpton, London.

LEES, D. H. and PAINE, C. G. (1958), "Lipoid Masculinizing Tumours of the Ovary", *J. Obstet. Gynæc. Brit. Emp.*, 65: 710.

LICHTENSTEIN, L. (1952), "Bone Tumors", Mosby, St. Louis.

LICHTENSTEIN, L. (1956), "Benign Osteoblastoma; Category of Osteoid and Bone-Forming Tumors other than Classical Osteoid Osteoma, which May Be Mistaken for Giant-Cell Tumor or Osteogenic Sarcoma", *Cancer (Philad.)*, 9: 1044.

LICHENSTEIN, L., and BERNSTEIN, D. (1959), "Unusual Benign and Malignant Chondroid Tumors of Bone", *Cancer (Philad.)*, 12: 1142.

MACCALLUM, W. G. (1936), "Textbook of Pathology", Saunders, Philadelphia and London: 1089.

MAYER, I. (1941), *Zur Histologie der Hidroadenome, Frankfurt, Z. Path.*, 55: 548.

MCDONNELL, W. V. (1956), "Myelolipoma of Adrenal", *A.M.A. Arch. Path.*, 61: 416.

MECHLER, E. A., and BLACK, W. E. (1943), "Gynandroblastoma of Ovary", *Amer. J. Path.*, 19: 633.

MENDELOFF, J. (1957), "The Olfactory Neuroepithelial Tumors — a Review of the Literature and Review of Six Additional Cases", *Cancer (Philad.)*, 10: 944.

MERIVALE, W. H. H., and FORMAN, L. (1951), "Case of Masculinovoblastoma", *Brit. med. J.*, 1: 560.

MEYER, R. (1931), "Pathology of Some Special Ovarian Tumors and their Relation to Sex Characteristics", *Amer. J. Obstet. Gynec.*, 22: 697.

MUMMERY, J. H., and PITTS, A. T. (1926), "A Melanotic Epithelial Odontome in a Child", *Proc. roy. Soc. Med.*, 19: Sec. Odont., 11.

NANGLE, E. J., and SYMMERS, W. ST. C. (1950), "Pleomorphic Sweat-Gland Adenoma of Foot", *J. Bone Jt. Surg.*, 32: 70.

NOVAK, E. (1947), "Gynecological and Obstetrical Pathology", W. B. Saunders Co., Philadelphia and London.

PLAUT, A. (1958), "Myelolipoma in the Adrenal Cortex (Myeloadipose Structures)", *Amer. J. Path.*, 34: 487.

ROTTINO, A., and MCGRATH, J. F. (1939), "Masculinovoblastoma; Primary Masculinizing Tumor of Ovary (So-Called Large-Cell Variety—Hypernephroid—Luteoma)", *Arch. intern. Med.*, 63: 686.

SCHILLER, W. (1939), "Mesonephroma Ovarii", *Amer. J. Cancer*, 35: 1.

SEVITT, S. (1956), "Benign Mesenchymoma in Finger", *J. Path. Bact.*, 71: 228.

SHELDON, W. H. (1941), "Myoepithelium in Sweat Gland Tumors; Distribution, Histology, Embryology and Function", *Arch. Path. (Chicago)*, 31: 326.

SHELDON, W. H. (1943), "So-Called Mixed Tumors of Salivary Glands", *Arch. Path. (Chicago)*, 35: 1.

SMETANA, H. F., and SCOTT, W. F. (1951), "Malignant Tumors of Nonchromaffin Paraganglia", *Milit. Surg.*, 109: 330.

STOUT, A. P. (1949), "Hemangiopericytoma; Study of 25 New Cases", *Cancer (Philad.)*, 2: 1027.

STOUT, A. P. (1956), "Tumors Featuring Pericytes: Glomus Tumor and Hemangiopericytoma", *Lab. Invest.*, 5: 217.

STOUT, A. P., and MURRAY, M. R. (1942), "Hemangiopericytoma; Vascular Tumor Featuring Zimmermann's Pericytes", *Ann. Surg.*, 116: 26.

SYMMERS, W. ST. C., and NANGLE, E. J. (1951), "Unusual Recurring Tumour Formed of Connective Tissues of Embryonic Type (So-Called Mesenchymoma)", *J. Path. Bact.*, 63: 417.

UNVER, R. Z. (1957), "On Thymolipomas", *A.M.A. Arch. Path.*, 64: 704.

WILLIS, R. A. (1948 and 1960), "Pathology of Tumours", 1st and 3rd Edition, Butterworth & Co., London.

WILLIS, R. A. (1958), "The Histogenesis of the Pigmented Epulis of Infancy", *J. Path. Bact.*, 76: 89.

WILLIS, R. A. (1958), "The Borderland of Embryology and Pathology", Butterworth, London.

WILLIS, R. A. (1959), "Modern Trends in Pathology", edited by D. H. Collins, Butterworth, London, Chapter 7.

ANTIBODY TO MURRAY VALLEY ENCEPHALITIS AND LOUPING-ILL VIRUSES IN AUSTRALIA AND PAPUA-NEW GUINEA.[1]

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MURRAY VALLEY ENCEPHALITIS (MVE) virus is believed to be a tropical virus which makes only irregular incursions into the temperate zone of Australia. Only six such epidemics have been reported in southern and eastern Australia since the first description of the disease in 1917 (Anderson, 1954; Anderson *et alii*, 1958).

In an effort to obtain more information about the occurrence of this or other Group B arthropod-borne viruses in tropical Australasia, two groups of sentinel chickens were stationed in the Northern Territory of Australia and New Guinea. The serological examination of these birds indicated viral activity in both groups during the year of observation.

The second part of this paper records the virtual absence of human antibody to louping-ill virus from 210 random human sera from eastern Australia and Papua-New Guinea.

Materials and Methods.

The virus of MVE was the strain isolated in 1951 (French, 1952). Stock virus was stored at −70° C.

The virus of louping-ill was the strain obtained originally from Moredun, and used in these laboratories by Burnet and Lush (1938). Fresh stock virus was prepared by two intracerebral passages in suckling mice, and then stored at −70° C.

Titration of these viruses and their antibody was as described for MVE virus (Anderson *et alii*, 1960).

Egg yolks were stored at −20° C. after arrival in Melbourne. Before use, they were thawed and diluted 1:6 in physiological saline. This dilution of yolk was tested for antibody in the same way as serum.

Sentinel chickens were chosen from flocks in Melbourne, and tested to confirm that they carried no serum antibody to MVE virus. They were transported to their destination in either New Guinea or the Northern Territory in mosquito-proof cages, and were thereafter so housed as to be fully exposed to local mosquitoes. The chickens were bled from the wing vein into sterile tubes. Sera were stored at room temperature for up to one week, and then at −20° C.

Murray Valley Encephalitis Virus.

Antibody in Papua.

On April 29, 1957, 80 sentinel chickens were distributed to five centres, 16 birds to each centre.

The centres chosen were two stations near Galley Reach, the villages of Edube and Motu on the Brown River, and Doura Village on the Vanapa River. All these places are within 50 miles of Port Moresby (Anderson *et alii*, 1960). Serum from each of the 67 chickens alive in August, 1957, contained no antibody to MVE. Between August 20 and 26, 1958, the following proportions of "positive" sera were found in screening tests with MVE virus: at Galley Reach, 0/6; at Edube, 1/6; at Motu, 5/12; and at Doura, 10/10. Each "positive" chicken had provided a "negative" specimen of serum in August, 1957.

The titres of positive sera were between 1:50 and 1:500.

Antibody in the Northern Territory.

In June, 1958, 80 chickens were distributed, in five lots of 16 birds each, to the Mission Stations at Goulburn Island, Roper River and Oenpelli, to the Welfare Department station at Beswick Creek, and to Humpty Doo. In November, 1958, and July, 1959, eggs were collected from 10 to 12 birds in each centre and carried to Darwin by air. Here, under the direction of Dr. J. M. Crotty, the yolks were removed to screw-capped jars and sent to Melbourne by air.

No antibody was detected in the yolks collected in November, 1958, and the only "positive" yolk in July, 1959, came from a bird at Roper River, The yolk was titrated to an endpoint of 1:54 against $100LD_{50}$ of MVE virus, and this result was confirmed twice.

Mildura, 1957–1958.

No clinical case of MVE was reported in the Murray Valley of northern Victoria during the summer of 1957-1958. Because local practitioners are acutely aware of this disease, the absence of reported cases is good evidence that there was no extensive epidemic during that summer. On the other hand, it would still be possible for the occasional sporadic case to be missed.

Greater significance may be attached to the results of an examination of strategically placed chickens for antibody to MVE virus. During the large epidemic in the Murray Valley in 1951, domestic chickens living near the river and its associated waterways showed an incidence of antibody as high as 70%.

On November 3 and 4, 1958, one of the writers (M.W.) visited Mildura, and with the cooperation of the public health inspector, Mr. P. Saunders, bled 76 domestic chickens living close to the river. All the birds had been alive since August, 1957, but no serum carried neutralizing antibody to MVE virus. This is believed to be reasonably good evidence that MVE virus was not active in the region between August, 1957, and October, 1958.

Other Records of the Activity of Group B Viruses.

An attempt has been made to summarize on one map the records of known or presumed activities of MVE virus (Figure I). In certain instances the available evidence could not distinguish between this virus and closely related agents such as Japanese B encephalitis virus. In the following brief summary of the literature, the numbers in parentheses refer to the same numbers on the map. Numbers 8 (Port Moresby hinterland) and 9 (Roper River) refer to the results presented above.

1. There seems little doubt that the epidemics of Australian X-disease in 1917, 1918, 1922 and 1925 were due to an agent closely resembling MVE virus (McLean and Stevenson, 1954). The distribution of these early outbreaks has been summarized by Anderson (1954).

2. The epidemic which occurred in the Murray Valley between January and April, 1951, is known to have spread at least as far north as Narrabri in northern New South Wales (Garven *et alii*, 1952). It was from this epidemic that the currently used strain of MVE virus was isolated (French, 1952).

3. Antibody studies in 1951 and 1952 indicated that MVE or a related virus had recently been active along the east coast of Queensland, at Mornington Island in the Gulf of Carpentaria, in the Northern Territory, and in New Guinea (Mackerras, 1951; Anderson *et alii*, 1952; Miles and Howes, 1953).

4. Miles and Dane (1956) obtained sera in the Northern Territory during the period from October to December, 1954. Of 29 domestic chickens aged 15 to 18 months, five carried neutralizing antibody to $50LD_{50}$ of MVE virus, and these workers concluded that between May, 1953,

[1] This work was carried out with the assistance of a grant from the National Health and Medical Research Council of Australia.

[2] Visiting Australia from the East African Virus Research Institute, Entebbe, Uganda, whilst in receipt of a World Health Organization Fellowship.

and December, 1954, MVE or a related virus had caused infections at Murray Downs Station near Alice Springs, and either at Darwin or at Beswick Creek. Human sera obtained at the same time gave results which were consistent with these conclusions.

5. As part of their serum survey in Queensland in 1955, Ludford and Cook (1957) tested the sera of seven horses, aged between 15 months and three years, for neutralizing antibody to MVE virus. All gave positive results, presumably owing to infection with a Group B virus between 1952 and 1955. The area of Queensland concerned extended from Spring Creek, north-west of Townsville, to the Mitchell River Mission on the Gulf of Carpentaria. At Spring Creek in May, 1955, they found two horses, aged 15 to 18 months, with a low level of complement-fixing antibody, and with neutralizing antibody to 100LD_{50} of MVE virus. These two animals must have been infected between February, 1954, and May, 1955. Confirmatory evidence was obtained from chickens bled at the Mitchell River Mission in June, 1958 (Doherty *et alii*, 1959). Neutralizing antibody was found in six out of seven chickens which had been alive since July, 1953, but not in 11 chickens introduced on to the mission in August, 1957.

6. In February and March, 1956, three patients with encephalitis were studied in Mildura. Sera were available from two; and these, together with the sera from 60 local chickens aged under 12 months, clearly showed that a Group B virus, probably MVE, had spread in the Mildura district during the summer of 1955-1956 (Anderson *et alii*, 1958).

7. During May, 1956, MVE virus was isolated from a native in Papua (French *et alii*, 1957). Sera obtained from four low-lying areas of Papua-New Guinea during the period from July to September, 1956, showed high-titre antibody to MVE and Japanese B encephalitis viruses (Anderson *et alii*, 1960).

10. Doherty, Carley and Trevethan (1960) placed sentinel chickens in north-western Queensland, around the Gulf of Carpentaria. Between November, 1958, and July, 1959, 15 of 56 birds developed Group B hæmagglutinin-inhibiting (HI) antibody, and a lower proportion of fowls developed neutralizing antibody to MVE virus. Sera from native children confirmed the presence of a Group B virus in the 12 months to July, 1959.

11. The same authors found that Group B HI antibody developed in nine of 11 sentinel chickens at Mitchell River Mission and neighbouring stations between February and April, 1960; and the presence of a Group B agent was also indicated by the fact that one of the research team at the mission developed HI antibody during March and April, 1960.

In southern Australia, each search for evidence of MVE virus has been concentrated in the Murray Valley, and principally in the Mildura district. This was the area of highest incidence of antibody during the epidemic of 1951, and it was in this region that the three human MVE infections occurred in 1956 (Anderson *et alii*, 1958). To prove the absence of an arthropod-borne virus from any area is difficult, if not impossible. Nevertheless, in the years between epidemics, both clinical and serological evidence pointed to the complete absence of the virus from Mildura and other centres in the Murray Valley. The years of presumed absence of virus were 1951-1952 (Anderson and Eagle, 1953; Reeves *et alii*, 1954), 1952-1953 (Anderson *et alii*, 1954); 1953-1955 and 1956-1957 (Anderson *et alii*, 1958). The present report adds the year 1957-1958.

Louping-ill Virus.

Louping-ill virus is classed with the virus of Russian Spring Summer encephalitis in a subgroup of the Group B arthropod-borne viruses, a subgroup which also includes Kyasanur Forest disease virus, recently isolated in Mysore, India (Work *et alii*, 1957).

The strain of louping-ill used in the present work was the only member of the subgroup available in this laboratory. It is of some interest that it had been stored since 1943 as a suspension of infected chorio-allantoic membrane, in a sealed glass ampoule at −70° C. In 1960 this stored material had an infective titre of 7·0 logs when titrated by intraperitoneal injection of 0·03 ml. in suckling mice.

Two hundred and ten human sera were screened for neutralizing antibody to louping-ill virus, serum diluted 1:6 being used. Only four sera neutralized the virus.

The 206 "negative" sera came from persons aged over 10 years, and living in the following areas in eastern and northern Australia: north, central and south Queensland (55 sera); the coastal belt of the Northern Territory (31 sera); Victoria (47 sera); also from the following areas in Papua-New Guinea: Lae and Wau (16 sera), the Sepik River (20 sera), the Aramia River (17 sera) and the Brown River (20 sera). They were collected between 1952 and 1959.

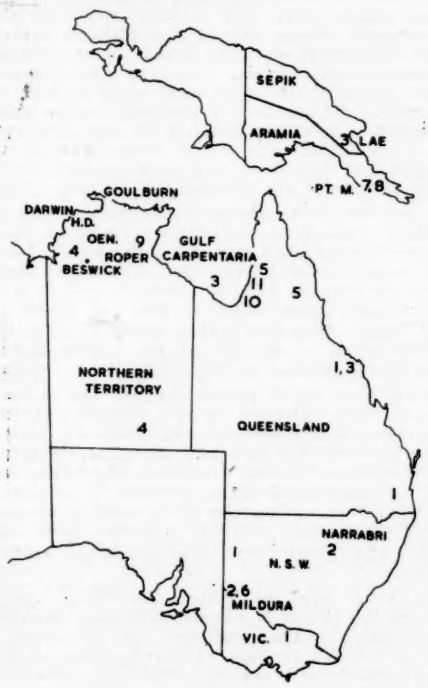

FIGURE I.

Map of Australia and New Guinea to show presumed presence of Group B arthropod-borne virus. 1, Australian X-disease, 1917-1925; 2, February-April, 1951; 3, prior to 1952; 4, May, 1953, to December, 1954; 5, February, 1954, to May, 1955; 6, February to March, 1956; 7, May, 1956; 8, August, 1957, to August, 1958; 9, June, 1958, to July, 1959; 10, November, 1958, to July, 1959; 11, February to April, 1960.

The four "positive" sera were obtained in 1952 from residents of Queensland or northern New South Wales. Titres were low, and three of the sera had similar low titres to MVE virus. The titres were, to louping-ill virus, 20, 8, 5 and 4, and to MVE virus, 15, 8, 6 and <4 respectively.

Discussion.

Eggs of wild birds were found to carry antibody to MVE after the epizootic in 1951 (Anderson, 1953), and McLean (1953) and Warner (1957) found that antibody titres against MVE virus were about the same in the serum of a chicken as in the yolk of the egg laid by that chicken. In the present study, because of the

geographical isolation of the mission stations in the Northern Territory, it was decided that collection of eggs would be a more practical proposition than the bleeding of chickens. The collection and titration of egg yolk were found to be quite feasible, but two practical facts emerged during the course of preliminary trials with birds immunized in the laboratory. First, many normal yolks inhibited the infectivity of MVE virus up to a dilution of 1:5 of yolk, but not beyond this; secondly, the level of antibody in the yolk of immunized chickens was approximately one-fifth of the titre of serum from the same bird. Thus, in any survey of avian antibody such as the present study, yolks must be diluted 1:6 for screening tests. Such tests will detect birds with serum antibody titres greater than about 1:30, but birds with serum titres less than this may be falsely classed as "negative".

The development of avian antibody to MVE virus in Papua indicated the activity of a Group B arthropod-borne virus in the hinterland behind Port Moresby between August, 1957, and August, 1958. Of the five areas sampled, Doura showed the highest incidence of antibody in sentinel chickens, and it is of some interest that this was the village where it was believed that the fatal case of MVE infection occurred in 1956 (French *et alii*, 1957). The finding of antibody in one yolk from the Northern Territory pointed to the activity of a Group B virus near the Roper River Mission between June, 1958, and July, 1959, and probably after November, 1958. These results are included in the map (Figure I).

Reference has been made above to the probable absence of Group B virus from the Mildura region in the years between 1951 and 1956, and also during 1957-1958. If this is accepted, it follows that Group B virus was active in the tropical zone of Australia and New Guinea during several years when it was not found in the Murray Valley. This conclusion supports earlier theories that MVE virus is enzootic in the tropics and makes only occasional excursions into temperate regions.

There is very little evidence about the intensity of Group B virus activity in the tropical Australasian region. The facts presented and reviewed here would be consistent with the idea that there were yearly peaks of virus activity; the only contrary suggestion we have seen is the observation made by Doherty *et alii* (1959) at the Mitchell River Mission on the Gulf of Carpentaria. In June, 1958, these authors bled 15 native children, aged two and three years, and found no antibody to MVE virus.

There must also be some uncertainly about the identity of the Group B virus or viruses responsible for the serological results presented and discussed above. Dengue is believed to have caused infection on the east coast of Queensland during 1925-1926, 1942-1944 and 1953-1955 (McCallum and Dwyer, 1927; Lumley and Taylor, 1943; Rowan, 1956, Doherty, 1957), and there were both clinical and serological suggestions that it spread along the coast of the Northern Territory in 1957 (McLean and Magrath, 1959). However, the overlap in neutralization tests between dengue and MVE is slight (Smithburn, 1954; Ludford and Cook, 1957), and we know of no records of dengue antibody induced in domestic chickens. For these reasons dengue seems an unlikely cause of the present serological results.

Apart from dengue, the only Group B arthropod-borne virus so far reported in Australia and New Guinea has been that of MVE, and the serological observations in New Guinea in 1956-1957 (Anderson *et alii*, 1960) and in the Mitchell River area of Queensland in 1957 (Doherty *et alii*, 1959), both recorded more sera "positive" to MVE than to its nearest relative, Japanese B encephalitis virus. This might reasonably suggest that MVE virus was dominant; but the possibility remains that some infections were due to Japanese B encephalitis or another similar virus.

Antibody to louping-ill virus was found in only four of 210 adult human sera, and then in very low titre. This may have been due to earlier infection with the virus of louping-ill; but the fact that the four sera also neutralized MVE virus to about the same titre as louping-ill virus suggested that both types of antibody might have been heterologous, possibly owing to infection with dengue. Thus the results of this limited survey neither confirm nor exclude the presence in Australia of virus of the louping-ill subgroup. The findings nevertheless may be of some value as a basis for further epidemiological work.

Summary.

Sentinel chickens developed neutralizing antibody to MVE virus in New Guinea between August, 1957, and August, 1958, and a similar response was found in one sentinel chicken at the Roper River Mission in the Northern Territory of Australia between June, 1958, and July, 1959.

Serological evidence of recent activity of Group B arthropod-borne viruses in Australia and New Guinea is summarized.

No significant antibody to louping-ill virus was detected in 210 human sera taken in northern and eastern Australia and in Papua-New Guinea between 1952 and 1960.

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References.

ANDERSON, S. G. (1953), "Murray Valley Encephalitis: A Survey of Avian Sera, 1951-1952", MED. J. AUST., 1: 573.

ANDERSON, S. G. (1954), "Murray Valley Encephalitis and Australian X-Disease", *J. Hyg.*, 52: 447.

ANDERSON, S. G., DOBROTWORSKY, N. V., and STEVENSON, W. J. (1958), "Murray Valley Encephalitis in the Murray Valley, 1956 and 1957", MED. J. AUST., 2: 15.

ANDERSON, S. G., DONNELLEY, M., STEVENSON, W. J., CALDWELL, N. J., and EAGLE, M. (1952), "Murray Valley Encephalitis: Surveys of Human and Animal Sera", MED. J. AUST., 1: 110.

ANDERSON, S. G., and EAGLE, M. (1953), "Murray Valley Encephalitis: The Contrasting Epidemiological Picture in 1951 and 1952", MED. J. AUST., 1: 478.

ANDERSON, S. G., PRICE, A. V. G., KOIA, N., and SLATER, K. (1960), "Murray Valley Encephalitis in Papua and New Guinea. II. Serological Survey, 1956-1957", MED. J. AUST., 2: 410.

ANDERSON, S. G., WHITE, J., and MCLEAN, D. M. (1954), "The Absence of Murray Valley Encephalitis Virus from the Murray Valley, 1952-1953", MED. J. AUST., 1: 113.

BURNET, F. M., and LUSH, D. (1938), "Infection of the Central Nervous System by Louping-ill Virus", *Aust. J. exp. Biol. med. Sci.*, 16: 233.

DOHERTY, R. L. (1957), "Clinical and Epidemiological Observations on Dengue Fever in Queensland, 1954-1955", MED. J. AUST., 1: 753.

DOHERTY, R. L., CARLEY, J. A., and LEE, P. E. (1959), "Studies of Arthropod-borne Virus Infections in Queensland. I. A Serological Survey of Aboriginal Missions Bordering the Gulf of Carpentaria", *Aust. J. exp. Biol. med. Sci.*, 37: 365.

DOHERTY, R. L., CARLEY, J. A., and TREVETHAN, P. (1960), "Fifteenth Annual Report of the Queensland Institute of Medical Research".

FRENCH, E. L. (1952), "Murray Valley Encephalitis: Isolation and Characterization of the Ætiological Agent", MED. J. AUST., 1: 100.

FRENCH, E. L., ANDERSON, S. G., PRICE, A. V. G., and RHODES, F. A. (1957), "Murray Valley Encephalitis in New Guinea. I. Isolation of Murray Valley Encephalitis Virus from the Brain of a Fatal Case of Encephalitis Occurring in a Papuan Native", *Amer. J. trop. Med. Hyg.*, 6: 827.

GARVEN, A. K., MARGOLIS, J., and FRENCH, E. L. (1952), "A Fatal Case of Murray Valley Encephalitis Occurring at Narrabri in New South Wales", MED. J. AUST., 2: 621.

LUDFORD, C. G., and COOK, I. (1957), "Murray Valley Encephalitis: A Survey of Human and Animal Sera in Queensland", MED. J. AUST., 2: 319.

LUMLEY, G. F., and TAYLOR, F. H. (1943), "Dengue", Service Publication No. 3, School of Public Health and Tropical Medicine (University of Sydney), Department of Health, Commonwealth of Australia.

MCCALLUM, F., and DWYER, J. P. (1927), "Dengue as a Cause of Death", MED. J. AUST., 1: 10.

MACKERRAS, M. J. (1951), "Encephalitis in Mornington Island" in "Sixth Annual Report of the Queensland Institute of Medical Research": 9.

MCLEAN, D. M. (1953), "The Behaviour of Murray Valley Encephalitis in Young Chickens", *Aust. J. exp. Biol. med. Sci.*, 31: 491.

MCLEAN, D. M., and MAGRATH, W. J. (1959), "Dengue in the Northern Territory", MED. J. AUST., 2: 719.

MCLEAN, D. M., and STEVENSON, W. J. (1954), "Serological Studies on the Relationship between Australian X-Disease and the Virus of Murray Valley Encephalitis", MED. J. AUST., 1: 636.

MILES, J. A. R., and DANE, D. M. S. (1956), "Further Observations Relating to Murray Valley Encephalitis in the Northern Territory of Australia", MED. J. AUST., 1: 389.

MILES, J. A. R., and HOWES, D. W. (1953), "Observations on Virus Encephalitis in South Australia", MED. J. AUST., 1: 7.

REEVES, W. C., FRENCH, E. L., MARKS, E. N., and KENT, N. E. (1954), "Murray Valley Encephalitis: A Survey of Suspected Mosquito Vectors", *Amer. J. trop. Med. Hyg.*, 3: 147.

ROWAN, L. C. (1956), "An Epidemic of Dengue-Like Fever, Townsville, 1954: Clinical Features, with a Review of the Literature", MED. J. AUST., 1: 651.

SMITHBURN, K. C. (1954), "Antigenic Relationship among Certain Arthropod-borne Viruses as Revealed by Neutralization Tests", *J. Immunol.*, 72: 376.

WARNER, P. (1957), "The Detection of Murray Valley Encephalitis Antibodies in Hen's Eggs", *Aust. J. exp. Biol. med. Sci.*, 35: 327.

WORK, T. H., TRAPIDO, H., NARASIMHA MURTHY, D. P., LAXMANA RAO, R., BHATT, P. N., and KULKARNI, K. G. (1957), "Kyasanur Forest Disease III", *Indian J. med. Sci.*, 11: 619.

VACCINATION IN INFLUENZA: PUBLIC HEALTH ASPECTS.

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INFLUENZA is the sole remaining pandemic plague that periodically terrorizes the world, and is the dread of all persons charged with the care of public health. It reappears in the form of an infection from different variants of the virus at various intervals, and sweeps in pandemic form across the world, gradually subsiding to localized outbreaks in the intervening years until the next variant appears.

The concept of "original antigenic sin" brought forward by Davenport and his co-workers (1953, 1957, 1958) and the discovery by Mulder *et alii* (1958) of A/Asian influenza antibody response in very old persons prior to exposure to the 1957 epidemic, have encouraged us to believe that there may be a limit to the antigenic variants of the virus, and that in the past 60 or 70 years we have seen the full cycle of variation and experienced all the antigenic components. However, for this we have no guarantee, and we live in fear of a new variant of high virulence and a repetition of the experience of 1918.

The shift in predominance from one variant to another, or the cyclic recurrence of variants, suggests the recurrent development in the population of a sufficient body of "non-immunes" to the particular antigenic structure of a variant and the consequent development of an epidemic caused by that virus. It is axiomatic that this body of "non-immunes" will occur in that portion of the population least subjected to contact with the various antigenic components of influenza viruses — namely, the younger age groups in the population.

The comparatively recent development of influenza vaccine awaited the advent of a new variant of influenza virus and a world epidemic for a test of its efficiency. This opportunity was afforded by the A/Asian influenza pandemic of 1957. The exhibition of a monovalent vaccine immediately prior to, or in the early phases of, exposure to infection has given different protection rates with different workers. Sigurjonsson *et alii* (1959) procured a 67% rate of protection, as did the Medical Research Council (1958). The Commission on Influenza (1957) procured a 42%-67% rate and Culver *et alii* (1957) procured a 43% rate. Results of this nature have encouraged the use of prophylactic vaccination, and as it is never known what next year's antigenic strain of virus is going to be, the routine use of polyvalent vaccine is being recommended, with as many known strains of virus antigens as possible included in the vaccine.

The initial appearance of antibodies and the rise in antibody level after vaccination are followed by a gradual decline, which indicates the necessity for annual booster doses. Public health authorities are therefore faced with the problem of deciding on the advisability of an expensive immunization campaign, and on the extent and frequency of such campaigns.

In order to obtain some information that might be of assistance in such decisions, advantage was taken of the opportunity offered for investigation by the A/Asian influenza epidemic in Western Australia in 1959. This was the second visitation of that strain, the first having occurred during the pandemic in 1957.

The Epidemic.

The epidemic occurred mainly in April, May and June, 1959. Prior to the epidemic there was an outbreak of an infection which was thought to have been caused by an adenovirus. An adenovirus was recovered from one case. However, by April, a clear clinical picture of influenza was presented, and many deaths in the elderly and a few in the very young were being recorded as the result of influenza, with such complications as bronchopneumonia, virus pneumonia, atypical pneumonia and acute myocardial toxæmia. A/Asian virus was recovered from several patients, and examination of paired sera indicated A/Asian influenza infection in more than 50% of the patients whose sera were examined. The adenovirus infection that appears to have been present would almost certainly, in a number of cases, have been confused at the clinical level with influenza, and so in the investigation that took place its presence would tend to reduce the apparent efficacy of vaccination.

The Investigation.

The investigation was carried out by means of a *questionnaire* designed to ascertain the incidence of influenza during the epidemic in the vaccinated staffs of Commonwealth Government departments compared with the incidence in the non-vaccinated staffs of State Government departments. Every effort was made to select State departments performing similar roles, or exposed to similar risk, to the Commonwealth departments. In addition, hospital staffs were interrogated, as these contained a proportion of vaccinated and non-vaccinated individuals, and one private organization that came in the same category was also investigated.

In time for analysis, 10,950 replies were returned, of which 8186 were from non-vaccinated and 2764 from vaccinated persons.

As diagnosis on medical certification is impracticable when such numbers are involved, and as such diagnosis during an epidemic is, in fact, scarcely more accurate than that presented by the patient, the criterion of diagnosis was "an influenzal type disease lasting for at least 3 days".

The Vaccine.

Prophylactic influenza vaccination in Commonwealth Government Departments commenced in 1955. The usual practice was to administer two initial doses at one month's interval and a booster dose annually thereafter. Table I gives the constituents of these vaccines in the various years.

Analysis of Replies to Questionnaire.

Of the 8186 non-vaccinated persons, 2911 or 35·6% claimed to have had an influenza-like disease during 1959.

Of the 2764 vaccinated persons, 1177 were vaccinated prior to 1958 and not subsequently vaccinated. They could therefore be considered inadequately protected, by virtue of both the time lapse and the inadequacy or absence of the A/Asian component in the antigen. In this group, 435 or 36·9% had influenza in 1959. The remaining group of 1587 vaccinated persons was comprised of 204 persons who had received two vaccinations in 1958 and none subsequently, 509 who received a booster dose in 1959, and 874 who received their first vaccination in 1959.

Of the 509 who received a booster dose, 77 received that dose prior to the end of March — that is, before the epidemic months of April and May — and the remaining 432 received the booster dose from April to June — that is, during the epidemic. The distribution of cases in the first eight months of 1959 was as follows: in January, 37 cases occurred; in February, 79; in March, 309; in April, 1308; in May, 1122; in June, 584; in July, 410; and in August, 63.

Of the 874 persons vaccinated for the first time in 1959, 122 received their first injection before the end of March and the remaining 752 during the epidemic. Table II shows the incidence of influenza in these various groups and the degree of protection obtained in the various states of vaccination.

Protection being calculated as the percentage of difference from the 35·6% infection rate in non-vaccinated persons, 34·3% protection was obtained in the previously vaccinated if the booster dose was given before the epidemic, and 19·9% if vaccination was given during the epidemic. In that group in which vaccination was given for the first time 5·6% protection was given if the first dose was given before the epidemic, but if the first dose was given during the epidemic there was evidence of a considerable lowering of resistance to infection, namely, a protection rate of minus 17·1%—that is, the infection rate in this group of 752 persons was 17·1% greater than in the non-vaccinated. It should be noted that in the system used in the recording, persons vaccinated during the epidemic may be shown in the vaccinated and infected group although the infection occurred in 1959 prior to vaccination. However, this cannot account for a higher rate of infection in those vaccinated for the first time during the epidemic compared with that in the non-vaccinated; the figures in this group, showing 314 infections in 752 persons compared with 2911 infections in 8186 non-vaccinated persons, are highly significant when tested statistically.

Of the 204 persons vaccinated in 1958 and not subsequently, 70 or 34·3% developed influenza in 1959, indicating a poor level of protection (3·6%) in an adult population a year after primary vaccination.

Before one proceeds to a discussion of these results, it is necessary to refer to a report by Duxbury and Keen (1960) on the same pan-Australian epidemic. In their paper a 60% protection rate is claimed for the same vaccine. However, in their *questionnaire*, they asked the interrogated persons to differentiate during the epidemic between influenza and upper respiratory tract infection, regardless of the bias that might have developed in the minds of the vaccinated as against the non-vaccinated towards the diagnosis of an infection subsequent to vaccination.

If influenza and respiratory tract infection are taken together, the published histograms of these workers suggest a protection rate of approximately 40% in May and less than 20% during the three epidemic months April, May and June. An account (Anonymous, 1959) has been given of the epidemic in Western Australia analysed in this paper. The claim is again made of a 60% protection rate. However, in that analysis vaccinated persons recorded infection subsequent to vaccination, and as vaccination proceeded throughout the duration of the epidemic, an examination of the relevant dates indicates that, on an average, the vaccinated were at risk for approximately half only of the duration of the epidemic. The 60% protection should therefore be reduced by that factor.

TABLE I.

Constituents of Polyvalent Influenza Vaccines Used by Commonwealth Government Departments from 1955 to 1959.

Year.	Constituent Types.	Number of C.C.A. Units.[1]
1955	A/Prime	Not measured.
	B/Tas./53	
1956	A/Prime	Not measured.
	B/Tas./53	
1957	A/W.A./56	200
	A/Asia/57	50–100
	B/Tas./53	200
1958	A/Asia/57	200
	A/Ned/56	75
	A/P.R./58	75
	A/Swine	50
	B/Tas./53	100
	D/Sendai	50
1959	A/Asia/57	200
	A/Ned/56	50
	A/P.R./58	50
	A/Swine	50
	B/Tas./53	150
	D/Sendai	50

[1] Chicken cell agglutination units.

It seems therefore that our figure of 34·3% protection is very close to the true protection rate given by complete vaccination with the polyvalent vaccine used in the 1959 pan-Australian epidemic.

Discussion.

The salient points for discussion are: (i) the low protection rate of 34·3% found in our series compared with the 67% protection rate found by the 1957 investigators; (ii) the poor result in persons vaccinated for the first time immediately prior to the epidemic; (iii) the bad results of vaccination in persons vaccinated for the first time during the epidemic; and (iv) the poor results in adults fully vaccinated a year prior to the epidemic, but not subsequently revaccinated.

There are two significant differences between this report and the published reports on the 1957 pandemic. The first difference is that the 1957 reports refer to the first recorded visitation of A/Asian influenza to the population examined, whereas the 1959 epidemic in Western Australia was a second visitation. The second difference is that the vast majority of the 1957 reports refer to the use of a specific monovalent vaccine, and not to a polyvalent vaccine in which the specific component is contained.

With regard to the first difference, it is reasonable to believe that, with repeated exposures to a new antigenic strain, the numbers of "immunes" or "relative immunes" in the population will increase, so that the difference in the proportions of infected to non-infected persons between vaccinated and non-vaccinated groups will decrease in direct relation to the frequency or duration of previous exposure. In other words, the apparent efficiency of a vaccine prepared for a new antigenic strain will be progressively less with each succeeding epidemic because of the rise in "natural immunes".

It is probable that the difference between previous estimates in the region of 60% and our present figure of 34·3% is partly due to this factor of recent previous exposure.

In an attempt to establish that a difference exists between a polyvalent and a monovalent vaccine exhibited during an epidemic or immediately preceding an epidemic which might affect the efficiency of the vaccine, recourse is made to the concept of the antibody-recall mechanism or "original antigenic sin". The predominant antibody response to vaccination against influenza is of a "booster"

TABLE II.

Incidence of Influenza Infection in Vaccinated and Non-Vaccinated Groups during Epidemic, April–June, 1959.

State of Vaccination.	Number of Subjects.	Cases of Influenza.	Percentage Protection.
Not vaccinated	8186	2911 (35·6%)	—
Vaccinated prior to 1958 ..	1177	435 (36·9%)	−3·6
Vaccinated in 1958—two doses and none subsequently ..	204	70 (34·3%)	3·6
Vaccinated in 1959:			
Group I (previously vaccinated):			
Booster dose given before epidemic	77	18 (23·4%)	34·3
Booster dose given during epidemic	432	123 (28·5%)	19·9
Group II (not previously vaccinated):			
First injection given before epidemic	122	41 (33·6%)	5·6
First injection given during epidemic	752	314 (41·7%)	−17·1

type directed against the major antigens of the strain of original infection, and it is possible that in the recall mechanism the original antigenic stimulus may preempt the antibody-forming sites and limit the response to new influenza-virus antigens. When therefore a new antigenic strain appears in the population, antibody response in infected individuals will be impeded by this preemption, and the exhibition of a polyvalent vaccine at such a time will enhance this preemption by further stimulating the antibody-recall mechanism of previous infection or vaccination, to the detriment of the formation of the antibody specific to the new antigen.

It would therefore seem a reasonable hypothesis that the poor result obtained in previously unvaccinated persons in the present investigation was due to stimulation by a polyvalent vaccine of the production of antibodies to original infection, to the detriment of antibodies required for this new experience. It follows, and this has been shown by Jensen and his coworkers, that broad immunological barriers against influenza-virus variants can be formed by vaccination most effectively in childhood.

Conclusions.

The investigation was undertaken to obtain evidence of the value of vaccination against influenza in the field of public health. Several conclusions may be drawn.

1. When a new antigenic strain of influenza virus appears in the population, a specific monovalent vaccine of sufficient strength provides good protection; but the apparent efficacy of this vaccine will decrease in succeeding years in proportion to the growth of active immunity developed in the population from repeated contact with the virus.

2. Where an epidemic from a new antigenic strain has developed or is about to develop, the exhibition of a polyvalent or non-specific vaccine is contraindicated, and only a monovalent specific vaccine should be used.

3. Broad-spectrum protection is produced most effectively in childhood.

These conclusions suggest that if any wide-scale plan of prophylaxis by vaccination is to be adopted against influenza as a general measure in non-epidemic periods, it would seem most profitable to give polyvalent vaccine in childhood to produce a broad-spectrum recall mechanism in that portion of the population which is most susceptible and most likely to provide material for the rapid spread of epidemics. Any subsequent vaccination as a general public health measure should be confined to vaccination of the population with a specific monovalent vaccine when invasion by a new or unfamiliar antigenic strain appears imminent or has occurred.

Summary.

In the second visitation of epidemic A/Asian influenza to Western Australia, the protection given to fully-vaccinated persons by a polyvalent vaccine containing 200 C.C.A. units of the specific antigen was in the region of 34%.

Adults vaccinated for the first time during the epidemic with the polyvalent vaccine had a higher infection rate than non-vaccinated adults.

Theoretical reasons are given for this, and conclusions are drawn regarding the role of vaccination against influenza in public health.

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References.

ANONYMOUS (1959), "Influenza and Absenteeism in the Commonwealth Public Service. Inoculation Programme in Western Australia", *Health (Canberra)*, 9: 125.

COMMISSION ON INFLUENZA, ARMED FORCES EPIDEMIOLOGICAL BOARD, UNITED STATES OF AMERICA (1957), "Vaccination against Asian Influenza. Basis for Recommendations and Preliminary Report on Efficacy", *J. Amer. med. Ass.*, 165: 2055.

CULVER, J. O., NITZ, R. E., and LENNETTE, E. H. (1957), "The Protective Effect of Monovalent Asian-Strain Vaccine against Asian Influenza", *J. Amer. med. Ass.*, 165: 2174.

DAVENPORT, F. M., and HENNESSY, A. V. (1957), "Predetermination by Infection and by Vaccination of Antibody Response to Influenza Virus Vaccines", *J. exp. Med.*, 106: 835.

DAVENPORT, F. M., HENNESSY, A. V., and FRANCIS, T., JUN. (1953), "Epidemiologic and Immunologic Significance of Age Distribution of Antibody to Antigenic Variants of Influenza Virus", *J. exp. Med.*, 98: 641.

DUXBURY, A. E., and KEEN, T. E. B. (1960), "Study in the Efficiency of Vaccination against Influenza in Two Employment Groups in Melbourne in 1959", *MED. J. AUST.*, 2: 206.

FOURTH PROGRESS REPORT OF THE COMMITTEE ON INFLUENZA AND OTHER RESPIRATORY VACCINES, MEDICAL RESEARCH COUNCIL (1958), "Trials of an Asian Influenza Vaccine", *Brit. med. J.*, 1: 415.

HENNESSY, A. V., and DAVENPORT, F. M. (1958), "Epidemiologic Implications of the Distribution by Age of Antibody Response to Experimental Influenza Virus Vaccines", *J. Immunol.*, 80: 114.

JENSEN, K. E., WOODHOUR, A. F., and BAILEY, A. A. (1960), "Immunization with Polyvalent Influenza Vaccines", *J. Amer. med. Ass.*, 172: 1230.

MULDER, J., and MASUREL, N. (1958), "Pre-Epidemic Antibody against 1957 Strain of Asiatic Influenza in Serum of Older People Living in the Netherlands", *Lancet*, 1: 810.

SIGURJØNSSON, J., SIGURDSSON, B., and GRIMSSON, H. (1959), "Experience with Influenza Vaccination in Iceland, 1957", *Bull. Wld. Hlth. Org.*, 20: 401.

THE SYDNEY FUNNEL-WEB SPIDER (ATRAX ROBUSTUS): III. THE NEUTRALIZATION OF VENOM BY HÆMOLYMPH.

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CERTAIN members of the class Arachnida are relatively resistant to the toxic effects of their venom. The scorpion *Buthus australis* has a resistance to the lethal action of its own venom which is 200 times greater than that displayed by the guinea-pig (Phisalix, 1922). Other

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species of scorpions possess a similar resistance (Nicolle and Catouillard, 1905; Shulov, 1955).

In the hæmolymph of scorpions there is a substance which neutralizes the toxic effects of venom. Metchnikoff (1905) reported that 0·1 ml. of hæmolymph was sufficient to neutralize *in vitro* an amount of venom which would kill a mouse in half an hour. More recently, Shulov (1955) also observed that the hæmolymph of *Leiurus quinquestriatus* neutralized venom *in vitro*.

In spiders, the neutralizing action of their hæmolymph has been less conclusively established than in the case of scorpions. Vellard (1936) observed that the hæmolymph of several species of spiders was toxic to pigeons, rabbits and mice. About 2 mg. of the hæmolymph of *Epeira* constituted the intravenous lethal dose for a rabbit (Phisalix, 1922). Because of this toxicity, only small amounts of hæmolymph could be used in experiments designed to show that hæmolymph neutralized the toxic effects of venom. By using sublethal doses of the hæmolymph of *Ctenus ferus*, Vellard (1936) was able to show that 0·1 ml. of hæmolymph neutralized *in vitro* one, but not two, minimum lethal doses of venom. He allowed the mixture to stand at room temperature for one hour before injecting it into a pigeon by the intravenous route.

The bite of *Atrax robustus* can be fatal to other funnel-web spiders (Wiener, 1959*a*). However, the cause of death in these cases may have been the trauma inflicted by the formidable fangs of the spider, which can penetrate the skull of a chicken (Wiener, 1957). No ill effects were observed when 2 mg. of spider venom were injected with a fine needle into the abdomen of *A. robustus*. Since the lethal dose for a guinea-pig weighing 250 grammes is about 2·3 mg. of venom given by the subcutaneous route (Wiener, 1957), the funnel-web spider, like the scorpion, appears to possess an appreciable resistance to the lethal effects of its own venom.

Since this resistance may be related to humoral factors, the action of hæmolymph on the venom of *A. robustus* was investigated.

Materials and Methods.

Adult female spiders were used for collecting hæmolymph. The legs of the anæsthetized spider were successively amputated at the proximal end of the femur, and the fluid (hæmolymph) which oozed out from the site of the cut was collected. About 0·1 to 0·2 ml. of fluid could be obtained from each spider. A white web-like coagulum formed in the hæmolymph shortly after it was exposed to the atmosphere. When hæmolymph was centrifuged, a clear, pale-blue fluid was obtained. This fluid was either used immediately after collection or was first freeze-dried. The amount of freeze-dried hæmolymph obtained from each of 30 female spiders ranged from 6 to 13 mg.

Venom was obtained by "milking" male spiders as described previously (Wiener, 1957). White mice weighing 15 to 20 grammes were used. All injections were given by the intravenous route.

Results.

Neutralization of Venom by Hæmolymph.

The intravenous injection into mice of either 0·5 ml. of freshly collected, or 10 mg. of freeze-dried, hæmolymph produced no observable ill-effects.

When 0·5 ml. of hæmolymph was incubated at 37° C. for 30 minutes with 2, 4 and 8 LD_{50} doses of spider venom respectively, the mixtures were no longer toxic. However, when similar amounts of venom and hæmolymph were injected immediately after mixing, all the animals died. Similarly, when freshly collected hæmolymph was heated at 100° C. for three minutes it no longer neutralized the toxic action of spider venom *in vitro*.

In order to determine the neutralizing power of hæmolymph more accurately, freeze-dried material was used. Varying amounts of hæmolymph dissolved in normal saline solution were added to 3 LD_{50} doses of venom. The mixtures were incubated at 37° C. for 30 minutes and then injected into mice. From Table I, it can be seen that with 0·45 mg. or more of hæmolymph the mixtures were no longer toxic.

In similar experiments in which shorter periods of incubation were used, it was found that at least 10 minutes must be allowed to elapse before any reaction between hæmolymph and venom resulted in a detectable loss of toxicity of the venom. In another experiment in which larger doses of venom were used, it was found that 6 mg. of hæmolymph neutralized at least 10 LD_{50} of venom. When a solution of freeze-dried hæmolymph was heated at 80° C. for 10 minutes, it no longer exerted any neutralizing effect.

Despite the appreciable neutralization of the toxic effects of venom which occurred when venom and hæmolymph were allowed to react *in vitro*, repeated attempts under varying conditions failed to demonstrate the occurrence of a similar effect *in vivo*. The intravenous injection of up to 10 mg. of hæmolymph did not protect mice against a subsequent injection of 2 LD_{50} doses of venom. At this stage, shortage of material prevented the use of larger doses of hæmolymph.

Specificity of Neutralization.

In order to test for the specificity of the neutralization of venom by hæmolymph *in vitro*, a few experiments were carried out with the venom of the red-back spider (Wiener, 1956) and with that of the tiger snake. No neutralization was observed when 2 LD_{50} of either of these two venoms were incubated with up to 8 mg. of the hæmolymph of *A. robustus*.

TABLE I.
Neutralization of Venom by Hæmolymph.

Amount of Hæmolymph (mg.).	Amount of Venom (mg.).	Number of Mice Injected Intravenously.	Number of Deaths.
—	0·10	2	2
0·11	0·14	3	3
0·22	0·14	3	3
0·45	0·14	3	0
0·90	0·14	3	0
1·80	0·14	2	0
3·60	0·14	2	0
3·60	0·20	2	0

LD_{50} of venom = 0·045 mg.

The hæmolymph of a few other species of spiders was also collected. In each case non-toxic amounts (0·1 to 0·3 ml.) of the hæmolymph of the different spiders were incubated with 2 LD_{50} of the venom of *A. robustus*. The mixtures were then injected into mice by the intravenous route. No neutralization occurred with the hæmolymph of spiders belonging to the families of Lycosidæ, Sparassidæ and Theridiidæ respectively. However, the hæmolymph of *Missullena occatoria* neutralized the venom of *A. robustus*.

Discussion.

The neutralizing action of hæmolymph is probably due to the presence of a heat-labile enzyme which occurs in relatively small amounts in hæmolymph. In view of the lack of antigenicity displayed by the toxic fractions of the venom of *A. robustus* in several species of animals, and the presence of at least one toxic fraction in venom which does not contain amino acids (Wiener, 1959*b*), it is unlikely that the neutralizing substance in hæmolymph is a true antibody. Such a view is also consistent with the failure of hæmolymph to confer protection *in vivo*, and with the time interval required before a mixture of venom and hæmolymph was rendered non-toxic.

More than 20 times the amount of hæmolymph which neutralized a given dose of venom *in vitro* failed to

protect a mouse from the lethal effects of a similar amount of venom. This failure of hæmolymph to neutralize the toxic action of venom *in vivo* contrasts with the apparent successful therapeutic use of the hæmolymph of the scorpion *L. quinquestriatus*. In a case reported by Adler *et alii* (1955), a volume of 2·3 ml. of hæmolymph collected from 35 scorpions was injected into an infant, aged 19 months, six hours after a sting had been sustained. At this time the patient was semi-comatose, but four hours later a marked improvement was noticeable and complete recovery eventually occurred. The mortality rate in infants from a sting by *L. quinquestriatus* is stated to be 75% (Adler *et alii*, 1955). One can, therefore, not be certain that in this case recovery would not have occurred spontaneously. On the other hand, one cannot exclude the possibility that the hæmolymph of the scorpion neutralizes the toxic effects of venom *in vivo* as well as *in vitro*. In addition, the absence of any added toxic manifestations when hæmolymph was injected into the infant indicated that in the amount used the hæmolymph of this species of scorpion is not toxic to man.

The hæmolymph of *A. robustus* also appears to be non-toxic to mice, although the hæmolymph of other species of spiders, unlike that of scorpions, has been reported to possess toxic properties (Phisalix, 1922; Vellard, 1936).

The hæmolymph of *M. occatoria* also neutralized the toxic action of the venom of *A. robustus*. This spider, although in a different family, belongs to the same sub-order (Mygalomorphæ) as *A. robustus*. The hæmolymph of other Mygalomorph spiders deserves further study.

No specific treatment is at present available for the treatment of funnel-web spider bites, which have caused at least seven fatalities in man (Wiener, 1959*a*). The lack of antigenicity of the toxic fractions of the venom prevented the development of a specific antivenene by methods which have been successful for the production of antivenenes again other venoms (Wiener, 1956, 1959*c*).

The isolation and concentration of the active substance in hæmolymph which neutralizes the toxic effects of the venom of *A. robustus* may yield a preparation which is effective *in vivo*.

Summary.

The hæmolymph of *A. robustus* contains a heat-labile non-toxic substance which neutralized the toxic effects of the venom of *A. robustus in vitro*.

The reaction between venom and hæmolymph required a period of at least 10 minutes, and no protective action was demonstrable *in vivo*.

References.

ADLER, S., BERMAN, S., SHULOV, A., and LEVI, N. (1955), "A Case of Scorpion Sting Treated by Intramuscular Injection of Hæmolymph of Leiurus (Buthus) Quinquestriatus", *Harefuah*, 49: 215.

METCHNIKOFF, E. (1905), "Immunity of Infective Diseases", Cambridge.

NICOLLE, E., and CATOUILLARD, G. (1905), *"Sur le venin d'un scorpion commun de Tunisie (Herometrus maurus)"*, *C.R. Soc. Biol.*, 58: 100.

PHISALIX, M. (1922), *"Animaux venimeux et venins"*, Masson, Paris.

SHULOV, A. (1955), "On the Poison of Scorpions in Israel", *Harefuah*, 49: 131.

VELLARD, J. (1936), *"Les venins des araignées"*, Masson, Paris.

WIENER, S. (1956), "The Australian Red Back Spider (Latrodectus Hasseltii). I. Preparation of Antiserum by the Use of Venom Adsorbed on Aluminium Phosphate", MED. J. AUST., 1: 739.

WIENER, S. (1957), "The Sydney Funnel Web Spider (Atrax Robustus). I. Collection of Venom and its Toxicity in Animals", MED. J. AUST., 2: 377.

WIENER, S. (1959*a*), "The Sydney Funnel Web Spider (Atrax Robustus). II. Venom Yield and Other Characteristics of Spider in Captivity", MED. J. AUST., 2: 679.

WIENER, S. (1959*b*), "Studies in Animal Venoms", Thesis, University of Melbourne.

WIENER, S. (1959*c*), "The Production and Assay of Stone-Fish Antivenene", MED. J. AUST., 2: 715.

Reports of Cases.

HÆMORRHAGICA HISTRIONICA — THE BLEEDING MÜNCHAUSEN SYNDROME.

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ASHER (1951) popularized the concept of Münchausen's syndrome in memory of the singular adventures of Raspe's artful baron, whose tall stories delight, as well as dismay, both young and old. Patients with the syndrome dismay, but seldom delight, those whose misfortune it is to misdiagnose their malady. Like Raspe's tales, the patients' stories may well stem from true histories, and, like that author, the story-tellers are mostly discredited, sometimes exiled and often despised. In more mundane vein, Chapman (1957) preferred the term "peregrinating problem patients", which emphasizes the psychiatric and socio-economic condition of these people.

Clyne (1955) suggested that the syndrome did not exist, only misdiagnoses, and that in this regard iatrogenic participation might be significant. Small (1955) suggested that an initial organic basis existed and that either there was no cure for the symptoms, or else an unnecessary, or unsuccessful, operation was performed. Psychopathic accretions then developed, either because the personality was galled by the disease or because frustration became an irritant, causing a psychopathic approach to life in general, and to doctors in particular. The following case history is published to illustrate an extreme example of the syndrome and some features of its development, and also to forewarn others. It occurred within a family affected by both hereditary osteogenesis imperfecta and a familial bleeding tendency.

THE APPARENT CLINICAL HISTORY.

The menarche occurred when the patient was 14 years of age and was followed by a regular 28 day cycle, with a four-day flow. She was married at 17 years of age, when pregnant. This pregnancy was complicated by intermittent vaginal bleeding from four months onward and a heavy blood loss at delivery. A second pregnancy ended in miscarriage with considerable blood loss at six and a half months, after recurrent vaginal bleeding; for this a blood transfusion was given. A third pregnancy also ended in miscarriage, after vaginal bleeding. After the first miscarriage, menstruation had become irregular, sometimes with heavy losses. (This history was not unexpected by the patient, because of her mother's history.)

At 19 years of age, the patient entered a district hospital for treatment of recurrent vaginal bleeding, suspected to be a miscarriage, but the toad test for pregnancy gave a negative result. Because of persistent bleeding her uterus was twice curetted and she was twice given blood transfusions, and was subsequently transferred to a base hospital, where her uterus was again curetted. In this hospital, the test for capillary fragility gave a doubtfully positive result and the platelet count was reduced. Dissatisfied with treatment, she took her discharge, but returned to the district hospital on account of further bleeding; this was treated conservatively with œstrogens, progesterone and blood transfusions. She was next transferred to the Brisbane General Hospital for investigation of a possible thrombocytopenia. On admission to hospital she was pale, agitated and sweating, with tachycardia and a hæmoglobin value of 12 grammes per 100 ml. On vaginal examination, the cervical os was seen to be patulous and blood was issuing from the internal os, resembling a menstrual loss. This blood loss was immediately increased by curettage. The patient doubted that her bleeding was menstrual at the time, but could not be

sure. On this admission to hospital the vaginal bleeding was said to be intermittent, mostly sudden in onset and profuse, rapidly saturating pads. While the patient was in a gynæcological ward the bleeding followed this pattern, but tended to occur when lights were switched off and after visiting hours, although it occasionally occurred at other times. She was subsequently transferred to a medical ward for specific investigation, but laboratory investigation failed to establish a cause for the bleeding. It seemed that a mesenchymal defect (on the basis of the family history) and a possible uterine abnormality were present.

At 20 years of age the patient entered another hospital (February, 1958) because of a heavy vaginal loss which drenched a bath towel; later bleeding appeared to respond to ergometrine and œstrogen administration. In addition, morphine was given repeatedly for pain and distress. Bleeding tended to occur at night, and on one occasion she was "soaked" with blood. At this hospital a fibrinogen deficiency was suggested as a possible cause, but this was not established. The patient subsequently returned to the Brisbane General Hospital in April, 1958, lying on blood-soaked bath towels, cold, pale and sweating, with tachycardia; because of shock she was immediately transfused with plasma, then with blood. Again, the vaginal bleeding was uterine in origin and increased immediately after curettage. Frequent transfusions were required and the patient began to develop fevers and rashes during their administration. Two months after her admission to hospital a small hæmatemesis — 50 to 60 ml. — occurred, and thereafter others, mostly preceded by pain, which was sufficiently intense to require morphine for relief. Later hæmatemeses were larger — 200 to 600 ml. — and the vomitus contained clots; the hæmoglobin level became low, but was not allowed to fall below eight grammes per 100 ml. After these hæmatemeses the patient seemed shocked, although her arterial blood pressure was variable, and transfusions seldom produced the expected increase in hæmoglobin concentration. Transfusions became a problem, with difficulty in the cross-matching of blood, transfusion reactions, thrombophlebitis and scars at the site of needle puncture, blockage of needles, apparently friable veins and transfusions "running into tissues". She appeared to have an irregular fever, partly related to the transfusions.

Her vomiting attacks were seldom followed by a precipitate fall in arterial blood pressure, and the vomitus seldom contained food if the vomiting occurred late at night, and was not acid. After a month of repeated hæmatemeses and transfusions, the hæmoglobin level was being maintained at 6·5 to 7·5 grammes per 100 ml.; after two months it was being maintained at 4·0 to 5·6 grammes per 100 ml. The vomiting attacks were observed carefully by both medical and nursing staff, as the diagnosis of Münchausen's syndrome seemed probable; they started as a dribble of blood, produced as if by regurgitation, and finally large volumes — up to 500 ml.—were vomited with heaving. Hunger-pains were complained of, and intense pain appeared to precede the attacks. An ulcer crater was recorded as having been detected on one barium-meal X-ray examination, although not on another, but the gastric mucosa appeared normal on gastroscopy. When vaginal bleeding and hæmatemeses were most severe, blood was present in the urine, but this was not so if the urine was collected directly from the urethra; its presence was apparently due to contamination. On one occasion the hæmoglobin level was increased to 17·7 grammes per 100 ml. by transfusion (the arterial blood pressure was 135/90 mm. of mercury), but within two days the level was 9·0 grammes per 100 ml. (blood pressure 106/65 mm. of mercury) and within five days it had fallen to between 3·5 and 4·5 grammes per 100 ml. (blood pressure 80/65 mm. of mercury), and all the signs of blood loss were manifested by the patient. As previously, laboratory investigations did not indicate a cause for bleeding, simply showing an intense iron-deficiency anæmia. Frequent feeding was resorted to because of the hunger-pains, but the patient later refused food and eventually, when restrained and sedated for complete rest, she staged a hunger strike, refusing treatment. Although she had been contemplating taking her discharge at the time, she finally did not do so.

Münchausen's syndrome appeared the probable diagnosis, but a mesenchymal defect with a bleeding tendency also seemed possible. In August, nodules appeared on the buttocks and finger-tips, and epistaxes recurred. There also occurred an episode of hysterical paresis, when intense conflict was experienced by the patient over proposed surgery, the care of her child and attempts to mortgage a farm for financing medical advice elsewhere. On her readmissions to the hospital, the resident staff did not doubt her collapsed state after blood loss. However, although the patient's mother claimed that her daughter did not give herself a chance to get better, the mechanism of the bleeding was not known.

In September, 1958, two other physicians cared for the patient. Nodular lesions appeared on the trunk, on the upper limbs, on the buttocks and on the thighs, and petechiæ occurred in crops over the breasts, the upper limbs and the hips. Microscopic hæmaturia was present, and although the hæmatemeses were less frequent, occult blood was constantly present in the fæces. Feverish chills occurred frequently, with an irregular fever. These physicians found difficulty in maintaining a diagnosis of Münchausen's syndrome, and because of the symmetrical nodular lesions and variable petechiæ, considered anaphylactoid purpura as a possible diagnosis. For this reason they instituted corticotrophin therapy. The lesions appeared to grow less with corticotrophin therapy, but the injections were disliked by the patient because of the considerable bruising. The hæmatemeses now consisted mostly of the vomiting of dark blood; complaints of abdominal pain were frequent, and morphine seemed essential to relieve the pain and to allay the restlessness associated with the bleeding. Again bleeding sites could not be found in the mouth, in the naso-pharynx or in the œsophagus, but during œsophagoscopy some blood clot was seen in the stomach. Transfusions were becoming increasingly difficult, with local thrombophlebitis presenting a constant problem. The hæmoglobin concentration was allowed to fall below four grammes per 100 ml., but the hæmatemeses continued. Accordingly, as œsophagoscopy showed blood clot within the stomach, a Pólya-type partial gastrectomy was performed, and at the same time a splenectomy also, for technical reasons. At operation, blood was seen throughout the lumen of the bowel, but subsequent examination of the stomach failed to reveal evidence of an ulcer past or present, or a convincing bleeding site. The spleen, enlarged to twice its normal size, showed reactive hyperplasia. The patient's convalescence was uneventful, except for a small hæmatemesis shortly after the operation, and she was not a troublesome patient. Later, a keloid-like scar worried her. Shortly after her discharge from hospital hæmatemeses recurred, and she was soon readmitted, when it was noted that the hæmoglobin concentrations fell out of proportion to the blood loss. Feverish chills continued, and morphine was frequently given, as distress and fear seemed always to accompany the vomiting. The patient criticized the failure of surgical treatment, and the nursing staff developed a feeling of helplessness concerning her, for nothing seemed to reduce the hæmatemeses. In November, 1958, for instance, after a period of anorexia, epigastric pain and then sudden weakness, she vomited 1000 ml. of blood clots on one occasion, and subsequent smaller amounts of blood. Immediately after the major vomit, the arterial blood pressure was 120/80 mm. of mercury and the pulse rate was 104 per minute. Subsequently large vomits were frequent, and the pain seemed particularly intense; the lowest recorded arterial blood pressure over this period was 75/55 mm. of mercury, and the highest pulse rate was 132 per minute. Gastroscopy and œsophagoscopy did not reveal a site of bleeding. Although intense sedation was obtained by

intramuscular injections of sodium phenobarbitone, and the patient slept most of the time, the bleeding continued. In December, 1958, vaginal bleeding, epistaxes (without evidence of trauma) and hæmatemeses were occurring together, and the hæmoglobin concentration was allowed to fall to between 3·0 and 3·5 grammes per 100 ml. At this time the patient showed definite signs of blood loss. Methylamphetamine hydrochloride ("Methedrine") was administered intravenously, but the patient was scarcely stimulated and talked but little, becoming restless, agitated and somewhat truculent subsequently.

As vaginal bleeding continued, a hysterectomy was performed on December 31, 1958. Although a proliferative endometrium had been obvious in the curettings of May, 1957, endometrium was not evident at operation; but there was chronic cervicitis, cervical endometriosis and, seemingly, an abnormal distribution of cervical blood vessels. The patient became troublesome in the post-operative period, particularly as busy nursing staff were not unduly sympathetic. She removed tension sutures because of discomfort and interfered with her wound. Hæmatemeses recurred within a few days of the operation and also vaginal bleeding, which was controlled by packs. She was finally discharged from hospital with a hæmoglobin value of 6·4 grammes per 100 ml., which did not increase during out-patient observation. In April, 1959, she was readmitted to hospital for transfusion because of continued anæmia. She was then febrile and apparently confused, and during her restlessness the transfusion set was pulled apart. Shortly after this admission she developed staphylococcal breast and pudendal infections, with abscesses that required incision. Repeated hæmatemeses — 100 ml. to 450 ml. — still continued and necessary transfusions were given after heavy sedation, as otherwise the transfusions either stopped or ran into the tissues. Each transfusion was now followed by an immediate rise in temperature and a rash, and later by thrombophlebitis; hæmatemeses were therefore expected, and prepared for, after the transfusions. Hæmoglobin concentrations averaged 7·5 to 10 grammes per 100 ml. before and after transfusion. Significantly, during one period in hospital there was an episode of hysterical coma, which was followed by depression.

In August, 1959, after a "cold" and the illness of her child, the patient's severe hæmatemeses recurred. With a low hæmoglobin value — approximately four grammes per 100 ml. — she had a hæmatemesis of at least 1000 ml., and a new transfusion officer administered urgent resuscitation measures. At this time she was being carefully watched for her method of blood loss, particularly as she had repeated hæmatemeses and was not as shocked as might be expected from the amount of blood lost and from her prior anæmia. A 16-gauge serum needle was found in her bed one night; although she was not told of this, she subsequently became agitated. Several nights later she was seen to prick her arm with another needle, producing multiple bleeding points, which were lesions she had not previously had. She was also attempting to puncture her veins, unsuccessfully and agitatedly. As she became acutely agitated when confronted, she was transferred to the psychiatric reception ward. When her locker was searched, the articles seen in Figure I were found; during previous searches, made when the patient was out of the ward, nothing suspicions had been present. Prior to transfer she was suicidal in intent, but she made only minor attempts, scratching her veins and wrists. On her transfer to the psychiatric ward her mood was variable; she was sometimes agitated, sometimes resistive and resentful. She also refused temporarily to eat, but she bled only once, when isolated, and the blood, produced presumably by spitting, was scarcely sufficient to spot a sheet. She was returned to the reception ward one month after discharge from the hospital because of barbiturate overdosage, but some of her later responses were hysterical; subsequently she became truculent and needed restraint.

She has been treated by other practitioners also, latterly in Victoria. She now claims to be suffering from anæmia, the result of a foot injury, which does not respond to parenteral iron therapy. She has given a history of a bleeding disease related to fragilitas ossium, of incurable anæmia and, to explain her operation scars, of a hysterectomy for an ectopic pregnancy and of a splenectomy for the relief of her familial bleeding

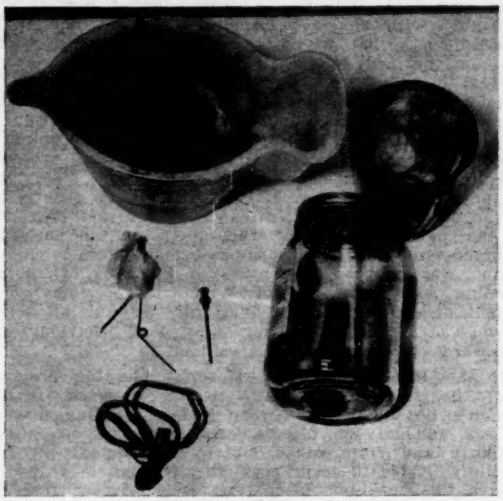

FIGURE I.

Articles finally found in the patient's locker. Blood was run into the plastic jug or glass beaker, preparatory to its dispatch home in the bottle. A simple tourniquet of elastic is shown, also needles.

disease. She has also added "congenital hypoprothrombinæmia", for which she takes "vitamin K" tablets. Hæmatological investigations at a Melbourne teaching hospital confirmed that no coagulation abnormality was present, and she was discharged from the hospital with a hæmoglobin value of 10·9 grammes per 100 ml. Subsequently she wrote an urgent letter to say that her "blood count was down to 50%" and she hoped that it was not thought that "I've been doing anything stupid as I have not". She also asked if iron therapy was unsuccessful whether a transfusion would be necessary.

THE FURTHER CLINICAL HISTORY.

Final details of this case and records from other hospitals became available only when the diagnosis was certain. Another patient had indicated her suspicions, but the patient's mother kept significant details to herself and prevented her son-in-law from voicing his doubts.

At the age of 14 years the patient had been an uncontrollable child and had run away from home on several occasions, staying at "a boy friend's house". Ultimately, she became a State ward and was committed to disciplinary care. In one children's home discipline caused her to revolt, in a second she was the ringleader of disorder and finally in a third, she "swallowed a pin accidentally" while working. She was then aged 15 years, and radiographs taken at the time showed a needle in the ascending colon, another in the transverse colon and a pin in the rectum. No longer virginal at the age of 17 years, she seduced her future husband, escaping from some of her difficulties through marriage. Her first pregnancy was successful, although it is doubtful if the child was really wanted, for it soon became a charge upon relatives. The second conception was certainly not wanted, and during this pregnancy the patient began to insert knitting needles into the uterine os in an attempt to induce the death of the fœtus. The recurrent vaginal bleedings in fact followed these manœuvres, and finally a miscarriage occurred. The

third pregnancy was also interfered with. Thereafter vaginal bleeding could be induced with ease; however, not all the apparent vaginal bleeding was produced in this way. On some occasions the patient stained perineal pads by spitting blood, after a sharpened finger-nail, needle or pin inserted between the gum and a back molar had produced sufficient bleeding for the purpose. This procedure, well known from another patient who presented with spurious hæmatemeses, was not finally adopted by the patient. Often stained perineal pads were left on the bed lockers. The failure to control the vaginal bleeding with œstrogens and gestogens at the district and base hospitals was understandable; there, as in other hospitals, the tablets were thrown away by the patient. During a curettage at the base hospital, a "pea-sized" tumour of the vaginal wall was resected, and found to be a subepithelial hæmorrhage. This was the only indication of an unsuccessful needle penetration of the uterus by the patient, and suggests her dexterity. In that hospital, bleeding subsequent to the curettage occurred only from the biopsy site and ceased when the vagina was packed; this presaged the type of vaginal bleeding which was to follow the hysterectomy. The patient discharged herself from this hospital, an action which was not typical of her subsequent behaviour, and afterwards she was refused treatment.

At the Brisbane General Hospital bleeding occurred from the vagina only until it was asserted, in the patient's hearing, that, if she had a bleeding disease, it was unusual for bleeding not to occur on sternal puncture and from other sites. The vaginal bleeding certainly tended to occur at night, although this was not always the case, but blood was seen issuing from the internal os on examination by gynæcologists and there was always increased bleeding after curettage, while the patient was anæsthetized. After there had been some comment on the unusual nature of her bleeding, hæmatemeses occurred, which were at first small in volume, later larger in amount. This bleeding led to more marked signs of blood loss and a significant anæmia. Blood was also added to the urine, although this was interpreted reasonably as accidental contamination from the vaginal bleeding; later, some hæmaturia was from definite urethral trauma. Some of the fevers were factitious, the patient falsifying thermometer readings by manipulation and friction; however, transfusions and thrombophlebitis contributed to some, although she confused nursing staff with her feverish chills. Some indurated lesions were at the injection sites; others were induced, rather than aggravated, by the patient. She developed a craving for morphine, but resented barbiturate sedation — these were not new symptoms. Her sleep habits were irregular and sometimes sleep was feigned. At this stage it was difficult to refuse transfusion, with the patient showing a frank anæmia and a hæmoglobin value below four grammes per 100 ml., although it was desired to know whether the bleeding would continue. The hysterical paresis seemed reasonably explained by her immaturity, her lack of education and the loss of her husband's farm on account of her illness. The alteration in the symptomatology when she was treated by other physicians might indicate the variable care with which petechiæ and skin lesions were sought for. Some petechiæ were produced by friction from clothing, and some others apparently by suction; in fact, the patient bruised easily, but bruises at injection sites were aggravated. Significantly, the contemplated gastrectomy and hysterectomy did not cure her self-inflicted disease.

The patient was also interfering with transfusions at night, actually running off blood from the donor set or her own vein into bottles, flasks and other receptacles so that she either performed a venesection during a transfusion or else did not receive the full amount of blood ordered. At such times she often pushed the needle through the vein, or allowed it to clot up. Blood obtained in this way was sent home by her mother, or by other relatives, but not by her husband, and stored in her room. Although some of the initial hæmatemeses were apparently faked by regurgitation of blood swallowed from a bleeding point in the gum, later ones were due to the vomiting of blood obtained at a transfusion and subsequently drunk; vomiting was performed with ease, and was quite convincing. The patient's husband finally admitted that he had often had to dispose of "stinking and putrefied" blood kept in billy cans, milk bottles and other receptacles after his wife had entered hospital on a number of occasions. Her mother had blandly given him to understand that "if her daughter sent the blood home the doctors must know about it, and let her, and it will be right"; hence, the husband failed to query the unusual circumstances of the blood store. Hæmatemeses were also faked by the patient's drinking blood from this stock, which explained some of the less fresh vomitus noted on her readmissions to hospital. In addition, her mother reported that the appearance of blood in the earth closet preceded her daughter's vaginal bleeding, and indicated that her daughter might be interfering with herself. At home the patient also performed venepunctures on herself, and a needle, which had originally been used for bovine immunization, and had disappeared from the dairy, was recognized by her husband among others purchased from a veterinary supplier. Throughout her illness she performed three types of venepuncture: (i) direct puncture of the veins followed by sucking; (ii) actual insertion of a needle into a vein, either at a recent transfusion site or elsewhere; (iii) utilization of an infusion needle. For each a simple tourniquet was applied. Thus, as the site of puncture was often that recently used for a transfusion, it is little wonder that transfusion sites were so frequently infected and that subsequent thrombophlebitis was so common, particularly as any precautions against infection were minor. These venepunctures were witnessed by another patient. Similarly, the frank abscesses were self-induced, like many of the earlier skin lesions.

Although the patient's locker was investigated on a number of ocasions when she was out of the ward (as it was obvious that she did not like others touching it), none of her equipment was found until she finally panicked. However, at this time she was having difficulty with venepunctures. Her attempted suicide seemed both a panic reaction and an hysterical one and was reminiscent of her state after the hysterectomy, when vaginal bleeding was prevented by packs and postoperative transfusions of blood were withheld. Her interference with the abdominal wound was ill considered, and she seemed critical of herself on this score.

Half-way through 1959 she professed reformation of a religious nature, and many people sought to help this sickly young mother and her child; indeed, it was difficult for them not to do so when told that the mother had leukæmia. As she was pale and often fell in the house from the effects of blood loss, leaving blood stains, many were sorry for the child. From these and others she stole money and clothes and to most people she told untruths; she also entered and stole from a neighbour's home. Finally, she attended a general practitioner, who saw her in charity, but from his surgery she took headed notepaper on which she wrote a prescription for barbiturates, and forged his signature. The dispensing pharmacist, although doubtful of the signature, nevertheless dispensed the barbiturates, and with these she attempted suicide, although her apparent "coma" responded too readily to therapy. Subsequently, the sequence of trauma and blood loss again led to an anæmia not responding to treatment.

The patient can marshal a list of diagnoses and treatments, partly based on fact, and with evident plausibility may well seek to delude others according to her previous pattern of behaviour.

The Personality of the Patient.

The patient lacked formal education, and a schoolteacher, who sought to befriend the family at one time, remembered her as a somewhat strange child, evasive

and difficult to understand, but not overtly naughty. An elderly cleric who knew the family well also remembered her as a strange child, oppressed by the family circumstances and by the mental and physical state of the siblings. He thought that the mother's deafness and her lack of insight and sympathy because of restricted contact were important factors in the child's waywardness. Later, his was the only visit in hospital that caused the patient any evident pleasure. She was rebellious and resentful of authority in the children's homes to which she was committed, and at the age of 15 years, a psychologist's report suggested that she had dull-normal intellectual ability. When tested, her performances were uneven, emotion was lacking and her grasp of reality was impaired; at times she denied seeing objects, stating that only reflections were seen, as objects did not appear real. At this age, it was suggested that she had psychopathic tendencies and a reasonably acute grasp of social situations, an ability she used for the fulfilment of her own desires.

She took her discharge from hospital on only one occasion, early in the illness, although she threatened this action at other times. Her manner was not truculent, showing rather a mixture of timidity and evasiveness which could have been accounted for by lack of education. She was basically unresponsive and sometimes withdrawn, especially if treated like a child. Distress was hard to evaluate but, significantly, it arose during corticotrophin therapy. With friends and relatives she was plausible and facile; she could also lie nonchalantly. Evident guilt, after entering a house and stealing, did not appear to dismay her, and she seemed to have little appreciation of personal and social responsibility or culpability. The loss of her husband's farm did not worry her; she was prepared to mortgage it from the first to seek hæmatological advice elsewhere. The trauma to her child, and the neglect, were not considered. She removed the little girl from loving care, placed her in less favourable circumstances and often barely noticed her at visiting time. In addition, she discussed the child's adoption because of her own incurable illness. However, suggestions that the child suffered from osteogenesis imperfecta were not acceptable. Her husband's disaster was not considered, and she preferred to desert him intermittently. She disturbed patients in the ward at night, sometimes by accident as she stole from their lockers, but on other occasions by design.

The reasons for the attempted abortions are not obvious, other than that they terminated unwanted pregnancies, but she claimed compulsion. Finally, it seemed that she procured definite self-satisfaction by her deceptions, particularly of doctors and nurses, although her illness served more obvious purposes in the beginning. While skilful in her deceptions, she never lost an evasive manner, which had suggested feigned illness at the onset. Her immaturity was obvious, and some of her responses to stress and personal disaster were suggestively hysterical.

DISCUSSION.

This patient demonstrates features of Münchausen's syndrome, presenting with a feigned bleeding disease (hæmorrhagica histrionica of Asher). She had convincing uterine bleeding, hæmatemeses and minor epistaxes. In addition, she attempted the addition of hæmaturia — at first by adding blood to her urine but later by urethral trauma — purpura and similar skin lesions. Infections were self-implanted, and factitious temperatures were recorded. Although the neurological symptoms were suggestively hysterical in nature, taken in conjunction with others displayed outside the hospital, particularly the falls and pareses, some may well have been part of the syndrome. She also had a craving for morphine, without strict dependence upon the drug. However, she seemed to resent drugs that dulled her senses or those whose action she did not understand.

The appearance of the patient after major hæmorrhages convinced the most sceptical that she had, in fact, lost blood. Her normal pallor and a translucent skin undoubtedly aided the deception. Also, it seemed obvious that the vaginal bleeding was uterine in origin and that the vomited blood did not come from an accessible bleeding point; the possibility of blood having been drunk was not considered. Initially, the failure of transfusions adequately to correct the anæmia was noted, as was the failure of the arterial blood pressure to fall commensurately with a hæmatemesis. However, later hæmatemeses appeared to result in an excessive fall in the hæmoglobin level. At the outset, and subsequently, the bleeding time (Ivy), clotting time, clot retraction and prothrombin time (one stage) were normal. Also, thromboplastin generation was normal, and there was no evidence of a circulating anticoagulant or of a fibrinolysin. However, it was the opinion in the hæmatological department that such tests did not categorically exclude a bleeding disorder; in addition, the partial thromboplastin time was not determined, but was subsequently shown to be normal. These results have been confirmed elsewhere. Also the patient was observed to bruise easily, and tests for capillary fragility gave positive results on several occasions; these are known features of osteogenesis imperfecta (McKusick, 1956). Hence, it was difficult to disregard completely a bleeding defect in view of the familial tendency, which there seems no reason to doubt, and its occurrence in other cases (Gautier and Guinand-Doniol, 1952).

Perhaps the patient lacked the flamboyancy of some other recorded examples (Chapman, 1957). However, the histrionic value of her symptoms was undoubted. Possible ætiological factors in the condition are given. First, the background of a diseased family and her attempted escapes from her circumstances and from parental control seem relevant; the psychopathic quality of her personality is evident, and a personality defect has occurred in other members of the family. Secondly, the adoption of a symptomatology compatible with the family history, particularly the miscarriages and uterine bleeding of the mother, seems significant; easy bruising and a local vascular abnormality of the uterine cervix aided her deception. To what extent uterine bleeding was ever spontaneous is not ascertainable, although some of the initial bleeding may have been. Thirdly, iatrogenic participation started with confused approaches to her bleeding and subsequently continued with suggestions that there was a fibrinogen deficiency, and that uterine bleeding alone was inadequate to establish a bleeding disease. Fourthly, her manual dexterity was considerable, and she watched all medical procedures carefully. Also, her appreciation of pain was convincingly less than that of other patients. Finally, the purposes of her illness are not clear, and the cost to herself and her family was proportionately great. She disliked farm life and lacked sympathy for her husband. A sense of achievement in deluding others, in stealing without apparent detection and in attracting sympathy seemed evident; remorse was absent.

In the period 1957 to 1959 (inclusive) she had at least 25 major admissions into six hospitals, the longest being for five months, representing a total in-patient time of at least 14 months. The nursing care required was disproportionately great, and the involvement of medical staff was considerable — as, for instance, in the time spent in examinations under anæsthesia and in operating theatres, and in the giving of more than 100 separate transfusions, of which many were set up more than once, as well as that occupied in routine clinical management of such a problem patient. With regard to blood transfusions alone, more than 110 litres of bank blood were used, representing more than 250 donors. The patient has travelled, within Queensland, from Cairns to Ipswich, and outside Queensland, to Melbourne. She constitutes a distressing example of the peregrinating problem patient (Chapman) or Münchausen's syndrome (Asher).

SUMMARY.

An example of Münchausen's syndrome is described. The features included induced uterine bleeding in pregnancy and afterwards, hæmatemeses after the drinking of blood, hæmaturia from blood contamination of urine and from urethral trauma, epistaxes and a variety of rashes, including pupuric lesions and infections. In addition, factitious temperatures, hysterical phenomena and antisocial behaviour were recorded. The personality seemed psychopathic and some factors in the production of the syndrome are discussed. The association of osteogenesis imperfecta and a bleeding tendency within the family is referred to.

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REFERENCES.

ASHER, R. (1951), "Münchausen's Syndrome", *Lancet*, 1: 339.

CANIGGIA, A., STUART, C., and GUIDERI, R. (1958), "Fragilitas Ossium Hereditaria Tarda: Ekman-Lobstein Disease", *Acta med. scand.*, 162: 340.

CHAPMAN, J. S. (1957), "Peregrinating Problem Patients—Münchausen's Syndrome", *J. Amer. med. Ass.*, 165: 927.

CLYNE, M. B. (1955), "Münchausen Syndrome", Letter to the Editor, *Brit. med. J.*, 2: 1207.

GAUTIER, P., and GUINAND-DONIOL, J. (1952), "*Un Syndrome Nouveau: La Maladie de Lobstein Associée à la Thrombasthénie familiale et héréditaire de Glanzmann*", *Schweiz. med. Wschr.*, 82: 407.

MCKUSICK, V. A. (1956), "Heritable Disorders of Connective Tissue. V. Osteogenesis Imperfecta", *J. chron. Dis.*, 3: 180.

SMALL, A. (1955), "Münchausen Syndrome", Letter to the Editor, *Brit. med. J.*, 2: 1207.

ADDENDUM.

Since acceptance of the original article for publication, further details have been obtained.

A definite alteration in personality occurred when the patient was transferred from a primary to a secondary school, antisocial activity becoming overt and appearing to reflect an "inability to make the grade". Frank lying was noticeable. She finally "left" school; also, she swallowed pins and "vomited" blood at one period of unrest. Gradually her behaviour became more antisocial, and paternity of the child was not accepted without question, reasonably, nor is it proven.

Recently her husband sent money for her return home, but this was used for travel elsewhere, as has happened in the past. She remains accepted by her own immediate family, alone; her eldest brother's example has not been helpful, and lately a sister has developed aimless behaviour.

APPENDIX.

Pedigree Chart of the Family.

Osteogenesis imperfecta was defined according to the criteria of McKusick (1956). Dominance within the family is evident and fœtal forms were included (Ekman-Lobstein-Vrolik disease).

The propositus (III, 3) had blue sclerotics, pale, translucent skin, abnormal scar formation, hyperlaxity of ligaments and short limbs; but she did not have increased fragility of bones or significant radiographic abnormality, and she was not deaf.

Osteogenesis Imperfecta.

FII.—The subject II, 2 has classical features of the disease and is totally deaf; II, 1 was stated to be more severely affected than II, 2, and II, 3 is stated to have blue sclerotics, but neither was examined.

FIII.—The sibship from II, 2 showed the highest concentration of affected individuals, some being grossly so (III, 4 and 5). Deafness is not evident in III, 8 and 9 but they have not attained the age of onset for deafness within the sibship.

FIV.—The subject IV, 3 has blue sclerotics and skeletal characteristics of the disease, without recurrent fractures.

Bleeding Tendency.

The bleeding tendency was defined descriptively. It refers to easy and excessive bruising, prolonged bleeding—after trauma and dental extractions—and epistaxis, in both sexes, and menorrhagia in females. This may be a feature of the

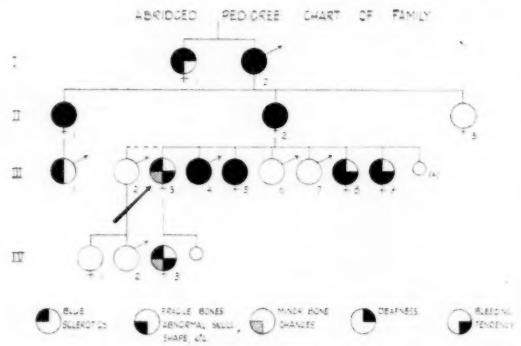

FIGURE II.

primary disease (McKusick, 1956), although others have regarded similar features as indicating the presence of Glanzmann's disease (Gautier and Guinand-Doniol, 1952; Caniggia, Stuart and Guideri, 1958). The informants were II, 2 and III, 5.

FI.—The subject I, 2 bruised easily and was subject to epistaxis.

FII.—The subjects II, 1 and 2 bruised easily, were subject to epistaxis and had prolonged bleeding after trauma; II, 2 had menorrhagia and excessive bleeding after miscarriages, of which she had a number. She was also subject to both ante-partum and heavy post-partum bleeding, needing blood transfusions after two deliveries; her deliveries tended to be premature.

FIII.—The subject III, 4 had a convincing bleeding tendency, and others were observed to bruise excessively; III, 3 and 4 were also subject to epistaxes.

FIV.—The subject IV, 3 was also observed to bruise excessively.

Personality Defects.

Personality defects were more difficult to define, but were evident within the family. For instance, II, 2 appears to have a blunted personality, with pride in her abnormalities and in those of her children. She is almost inaccessible because of her deafness, which has restricted the maternal influence within the home. In her children, educational deficits are present, but some personality defects appear not to be educational. The subject II, 5 has good scholastic attainment; II, 3 lost schooling and was required to protect her severely affected sibs at an early age.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Treatment of Emotional Problems in Office Practice", by Frank F. Tallman, M.D.; 1961. New York, Toronto, London: McGraw-Hill Book Company, Inc. 8″ × 5¼″, pp. 446. Price: $11.00.

"Dietary Proteins in Health and Disease", by James B. Allison, Ph.D. and William H. Fitzpatrick, Ph.D.; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications Ltd. 9″ × 6″, pp. 96. Price: 36s. (English).

The Medical Journal of Australia

SATURDAY, MARCH 25, 1961.

THE AUSTRALIAN CANCER COUNCIL.

FOR many years cancer, and with it the investigation of normal life processes, has attracted more research workers than perhaps all other disease processes combined. There have been some notable monetary contributions from governments, but in the main finance for this type of research has come from voluntary bodies, such as the British Empire Cancer Campaign in Great Britain and the American Cancer Society in the United States. In addition to research, this type of fund has provided facilities for actual treatment where these have been required, and this has probably applied in particular to the establishment of facilities for radiotherapy of various types, for which purpose there have been public gifts of large quantities of radium as memorials, such as has occurred in Great Britain and in Sweden. Particularly in the United States, the voluntary funds have also supplied services for patients suffering from cancer, such as hospitals, hostels, transport services, home nursing and the like. In recent years there has been some attempt at coordination of these services by the formation of an International Union against Cancer, comprising member countries who contribute an annual subscription of what they feel they can afford, while the Union has encouraged smaller anti-cancer bodies within the various countries to join as associates. It organizes an International Cancer Conference every three years and in general attempts the coordination of research and possibly treatment.

In Australia there has been the same combination of financial help from governments and from public subscription. In 1928 the Federal Government divided 10 grammes of radium between the various teaching hospitals in Australia, and several of the State Governments have provided equipment for radiotherapy to supplement the cancer treatment already being carried out efficiently by the various surgeons of this country. But, as happened overseas, in some areas in Australia such equipment was provided from funds subscribed by the public; in South Australia, for example, in 1929 deep X-ray equipment was provided by the Anti-Cancer Committee for the establishment of the first radiotherapy department in the Adelaide Hospital. In some States research has been supported from government funds, while in other States public subscription and charitable bequests have been used to provide the necessary finance. Good work has obviously been done, but in all of this there has been no coordination of effort between the several States.

Hoping to effect some coordination, but perhaps not quite clear as to how this coordination might best be used, Sir Peter MacCallum, of Melbourne, Dr. John Mayo, of Adelaide, and Dr. R. J. D. Turnbull, the Minister of Health in Tasmania, in 1955 arranged for the Commonwealth Department of Health to call a conference of all interested bodies in Australia. At this conference it was suggested that an Australian cancer body should be formed and that it should be supplied with funds raised by the anti-cancer bodies in the various States, such funds being allocated on the basis of 60% to the State body and 40% to the national body as is done in the United States for the American Cancer Society. It was probably the suggested allocation of funds which caused this attempt to break down, for while in one of the major States anti-cancer funds are supplied by a generous annual grant from the government, in some other States such anti-cancer funds are raised from time to time by public subscription, and there could obviously be a very great discrepancy in the amounts paid to a central organization. In addition, it was clearly stated at this conference that no Commonwealth finance was available for this project and the attempt to form a national body was abandoned.

In the belief that interstate coordination in cancer affairs was essential rather than desirable, a further meeting of the various State cancer bodies was arranged in Melbourne in August, 1960, during the time of the Victorian Cancer Congress. It was here suggested that a somewhat different approach to unity would be practicable, with the States retaining their local autonomy, and a national body provided with its secretariat and the necessary funds by a per-capita contribution from the various States. It was agreed that such a body could help prevent duplication of research in Australia, it could coordinate a research project throughout the whole Commonwealth to use clinical material which might not be adequately available in any one State, and it could prepare material for public and professional education, prepare material for use by the individual States in fund-raising and represent Australia in the International Union against Cancer. It was agreed to meet again in November, 1960, after discussion by the various State instrumentalities, the expenses of the November meeting being generously supplied by the Anti-Cancer Council of Victoria. This meeting, representative of all Australian population groups except those under the control of the Commonwealth Government, expressed unanimous agreement with the proposition, and the members present formed themselves into the first Council of the Australian Cancer Council; the desirability of having equal representation of lay and medical people on this Council was stressed, and Councillor W. J. Kilpatrick, of Melbourne, was elected the first chairman, with Dr. B. S. Hanson, of Adelaide, as vice-president.

It is not expected that there will be any dramatic change in cancer control and treatment as a result of the formation of this committee, but there will undoubtedly

be some solid work performed by it, with pooling of ideas between the various States and in many cases a saving of duplicated effort. The necessary legal formalities are at present in progress, after which there will obviously be an attempt to enlist suitable people in a national secretariat and the real work of this Council will begin. Its formation appears to be a constructive approach to a most important matter, made only after much careful thought and consideration of the many factors involved. We wish it well and will await reports of its future activities with interest and confidence.

Current Comment.

CARCINOMA OF THE ŒSOPHAGUS.

THE treatment of carcinoma of the œsophagus is a subject which has received much attention, but the results are still too often disheartening. The skill and ingenuity of the ablest surgeons have been applied to the devising of heroic operations for the removal of such growths, but though much has been achieved, these operations still carry a formidable mortality rate, and recurrence among the survivors is frequent. In the face of such results some surgeons face the problem with a degree of resignation which might be called defeatist. In a paper by M. M. Ravitch of the Johns Hopkins Hospital and others,[1] the authors conclude with the statement:

> The results of the operative treatment of carcinoma of the esophagus are disappointing in terms of survival and of cure rates. The organ is fundamentally so situated, and the disease of such a character, as rarely to lend itself to cure by operative means. It seems justifiable therefore to direct our efforts toward palliation rather than cure and to seek the methods which will yield the best results in terms of patient months of comfort, with deglutition restored.

Partly in protest against such resignation, E. E. Dunlop has reviewed his own series of cases[2] and those seen at the Royal Melbourne Hospital during the past decade. Like other writers on this subject, he emphasizes that the difficulties in the treatment of carcinoma of the œsophagus arise not only from the formidable nature of the disease, but also from the fact that many of the sufferers are old and frail. In the Royal Melbourne Hospital series the average age was 66 years in males and 65 years in females, figures which agree closely with those of other authors. Dunlop reproduces a table published by W. T. Moss in 1959, which shows the results of treatment of carcinoma of the œsophagus in 14 centres (in Britain, America, Sweden and Japan) which have reported their survival figures for all patients seen. Out of a total of 6348 patients 90 survived for five years after treatment; 50 of these survivors had been treated by surgery and 40 by radiotherapy. The proportion of patients treated by surgery at different centres varies greatly; of the surgically treated series the most remarkable is that of K. Nakayama of Japan, who has performed 399 resections, with an operative mortality rate of 5·3% in cases of carcinoma involving the lower third of the œsophagus and 13·8% in cases of carcinoma of the middle and upper thirds, and claims 18 five-year survivals out of the 50 in Moss's table.

Dunlop reports on the results in 170 of his own patients and in 138 patients treated at the Royal Melbourne Hospital, the two series partly overlapping. In his own series resection was performed in the very high proportion of 68% of all cases seen (Nakayama had operated on only 31% of patients seen at Chiba), with an operative mortality of 28% (15% for carcinomas in the lower third, 32·5% for those in the upper two-thirds). Of 91 patients seen more than five years ago, resection had been performed in 68 cases, and 18 of the patients had lived for more than five years. Radiotherapy does not appear to be favoured as a first approach in Melbourne, and Dunlop states that no long-term survival in such cases has been observed at the Peter MacCallum Clinic, except in two cases in which radiotherapy was used for the treatment of local recurrences after primary surgical excisions.

Dunlop considers that on the basis of results obtained in Melbourne there does not appear to be any well-established case for abandoning surgery for carcinomas of the upper two-thirds of the œsophagus. He comments that a survey of these results, together with those available from other countries, suggests that the disease is grim indeed, but believes that surgery offers comfort and some distinct hope of lasting relief.

[1] *J. thorac. Surg.*, 1952, 24: 256 (September).
[2] *Aust. N.Z. J. Surg.*, 1960, 30: 81 (November).

BREAST FEEDING AND ARTIFICIAL FEEDING.

INFANT FEEDING is a subject of considerable interest to a large number of people, including family physicians, pædiatricians, infant welfare nurses and, not the least, mothers. A modern investigation[1] designed to determine the relative merits of breast and artificial feeding warrants close scrutiny. Numerous claims have been made for the superiority of breast feeding but, as the authors of this report point out in their review of the literature, sociological and environmental factors play such an important role in artificial feeding that the relative merits of each method can be determined only against specified social backgrounds. This same comment is also made by the authors of the Norbotten Study,[2] which should be read in conjunction with the British study. The marked improvement in community, kitchen and personal hygiene in many countries in the last half century makes it essential to obtain current information if a comparison is to be made. The investigation reported here covered 744 infants and was made in the three and a half years from March, 1947, to October, 1950; 521 of the infants were full-term and 223 were premature; all were delivered at the Mothers' Hospital, London. At the time there was full employment, so that there should have been no economic bar to satisfactory infant feeding. The fully breast-fed infants were weaned between six and seven months of age on to full-cream milk.

Part I deals with the weight gains and hæmoglobin levels of full-term and premature infants. The weight gains, hæmoglobin values, etc., of the full-term infants were equated against National Standards and previous studies by various authors, and it was concluded that the group studied represented a satisfactorily healthy group which could be used for comparisons with the premature group. Amongst the most interesting observations were the relatively small gains in weight and the retarded ossification of premature infants given human milk. They also gained more slowly than the fœtus in utero of the same gestational age; the retardation in growth was most pronounced in the infants smallest at birth. The conclusion that "human milk is an inadequate feed for small premature babies in early life" must come as a surprise to some doctors; however, the protocols support this conclusion.

As a result of this investigation the authors make suggestions about the protein requirements of infants. They conclude that for an infant weighing under 4·5 lb.

[1] "Weight Gains, Serum Protein Levels and Health of Breast Fed and Artificially Fed Infants, Full Term and Premature", Privy Council, Medical Research Council Special Report Series, No. 296; 1959. London: Her Majesty's Stationery Office. 9½" × 6", pp. 164, with 68 tables and 69 figures. Price not stated.
[2] Mellander, O., Vahlquist, B., Mellbin, T., *et alii* (1959), "Breast Feeding and Artificial Feeding. A Clinical, Serological and Biochemical Study in 402 Infants, with a Survey of the Literature", *Acta pædiat. (Uppsala)*, 48, Suppl. 116.

at birth, the protein requirement is not less than 1·7 to 2·0 grammes per pound per day, compared with that of a normal full-term infant, which is about 0·85 gramme per pound per day. This makes interesting reading beside the opinions of Holt[3] and of Gordon and Garzon[4] that the protein requirements of full-term infants were between 2·5 and 3·5 grammes per kilogram (1·1 to 1·6 grammes per pound per day) of body weight.

Parts II and III report studies on serum protein levels in full-term and premature infants, and the results are correlated with birth weight and feeding methods. Perhaps the most significant finding was the sharp fall in serum globulin level of about 20% in the first five weeks of life. The level remained stationary to the age of about four months, and although a slow rise occurred, even at 18 months the levels were below adult values. By following the serum levels of the various fractions of protein in premature infants of different gestational ages, these workers were able to conclude from the steady rise in serum albumin and globulin levels that the fœtus is able to synthesize its own plasma proteins with the exception of gamma globulin, which is probably of maternal origin. There is a sharp rise in gamma globulin level in the last two months of fœtal life, corresponding to the greater permeability of the placenta. In this respect it is of interest that the Norbotten Study revealed that at the age of 7·5 months the serum gamma globulin level of early weaned infants was statistically significantly higher than that in the infants fully breast-fed to that age.

The report of the British study not only presents an account of the carefully planned observations of the authors, but provides an exceedingly full review and interpretation of the literature on the relative merits of breast and artificial feeding, and demonstrates the advances that have been made in this topic in the last 20 years. Because of the importance of the subject, these two reports are commended to doctors who take more than a casual interest in the problems of infant feeding.

UPROOTING AND RESETTLEMENT.

AUSTRALIA'S future development will depend upon continuing migration of people from overseas and their resettlement here. Many problems arise when large numbers of people move from one part of the world to another; but apart from the demographers and social scientists of the Australian National University, few people in this country seem to have been taking these problems as seriously as they might. The medical aspects of migration have barely been glanced at. In line with this situation is the fact that at a meeting of the World Federation for Mental Health in 1958 on the subject "Uprooting and Resettlement"[1] only one Australian (Sir Harry Wunderly) spoke, and then only to present the official views of the Department of Immigration. The only scientific paper about Australian immigration was by an American; its impartiality at least adds to its interest.

Apart, however, from the fact that it should stir our consciences, the report of the meeting contains much else that should interest Australian doctors. The use of the word "uprooting", the echoing memories of Hungary and preparations for World Refugee Year led many contributors to devote much of their time to the special problems of refugees; but some speakers clearly realized that voluntary migrants have their problems too. Professor Sawatsky of Toronto, for example, spoke in general terms of the assimilation of immigrants in that city, and most of his remarks apply equally to conditions in this country. An anthropologist's impressions of the extraordinary amalgamation of humanity in Israel make an interesting contrast. The addresses of Brock Chisholm, a great humanist and medical statesman, of the social scientist, Maria Pfister-Ammende, of Erik Erikson, himself an "uprooted" psychiatrist, and of Hans Hoff, the president of the meeting, are all outstanding contributions which deserve close study.

Psychiatrists and social scientists are often reluctant to produce meaningful numerical data, preferring weight of words to make their points. But there are some sobering statistics in this book: 600,000,000 out of a total 900,000,000 children in the world are hungry and sick; 40,000,000 people have been forcibly uprooted from their homes since 1945; and the well-known figures on the population explosion are here. We would have liked to see also comparative figures, which the Intergovernmental Committee for European Migration must surely have, of migration since 1945 to Canada, South America, Southern Africa, Australia and New Zealand, though perhaps this is not the place to expect them. One is left with the thought that a more critical approach to the medical problems of migration would be very desirable in Australia.

[3] *J. Pediat.*, 1959, 54: 496.

[4] *J. Pediat.*, 1959, 54: 503.

[1] "Uprooting and Resettlement", World Federation for Mental Health; Eleventh Annual Meeting of the World Federation for Mental Health, Vienna, Austria, August, 1958; 1960. London: H. K. Lewis & Co. Ltd. 8½" × 6", pp. 150. Price: 10s. net (English).

ARTIFICIAL RESPIRATION.

IN recent years there have been many discussions and articles on artificial respiration and the best methods of performing it, particularly in acute emergencies without the help of special apparatus or experienced persons. Of particular interest is such a discussion by members of the United Services and some American and Canadian visitors.[1] Professor Ronald Woolmer, of London, speaking of first aid in acute respiratory failure, emphasizes the need to concentrate on ventilation — on restoring the bellows action of the chest — leaving the circulation to respond to this indirect method of helping it. "I do not, he states, "believe that a block to diffusion is often of importance." In his view a combination of the two methods, squeezing and pulling, is better than either alone. In the human subject Holger-Nielsen's method is more efficient than Schafer's, but any obstruction will defeat every method of artificial respiration. Woolmer points out that water is rapidly absorbed from the lungs if there is still some pulmonary circulation. There is usually some leakage with the positive pressure methods, e.g., the mouth-to-mouth method, and to compensate for this at least one litre must be delivered with each breath. "The adoption of the supine position for the positive method is not a disadvantage."

Surgeon-Lieutenant J. Cox, R.N., reminds us that the Royal Humane Society abandoned expired-air resuscitation in 1812 because the expired air was considered poisonous. Expired-air resuscitation has proved to be very efficient, and no respiratory acidosis occurs. It has the great advantage of being easily taught. Pressure of about 50 cm. of water can be obtained by this method; this is an advantage in the presence of low lung compliance, but it should be remembered that pressure above 25 cm. of water in infants may cause damage.

To illustrate the efficiency of mouth-to-mouth breathing, Squadron-Leader Merrifield states that when hæmoglobin saturation has fallen to 75% in apnœic persons, it is restored to 96% in about eight breaths—"almost as quickly as flushing patients with oxygen". Stress is laid on the importance of placing the head in the hyperextended position to provide an open airway.

Major-General Hilton-Sergeant offers a warning on the meeting of possible damage by untrained persons using an artificial airway and of some of the disadvantages of the supine position, e.g., regurgitation of stomach contents. Professor Woolmer's reply to this is that there is little chance of damage from an artificial airway if it is a properly designed one.

[1] *Proc. roy. Soc. Med.*, 1960, 53: 311 (May).

Abstracts from Medical Literature.

SURGERY.

Small Bowel Atresia.

O. SWENSON AND J. H. FISHER (*Surgery*, May, 1960) present a study of 12 consecutive cases of small bowel atresia, which they state is one of the more common congenital anomalies causing intestinal obstruction in the newborn. Up to 1950, only 20 cases of survival had been reported in infants with this lesion, but recent major advances in the management of intravenous therapy, the control of serum electrolytes, anæsthesia and antibiotics have contributed to the lowering of the mortality rate. Patients are also referred earlier for operation. Several methods of operative management have been suggested, but the authors consider that resection and primary end-to-end aseptic anastomosis is the preferred procedure for this lesion. They state that in their experience this procedure has been relatively safe and followed by a relatively uncomplicated post-operative course. Two of their patients died, one of whom weighed only 4 lb. 1 oz. at birth. Four of the infants had other anomalies which complicated their management. The author's technique is fully described and illustrated.

Pseudocysts of the Pancreas in Infants and Young Children.

C. T. OECONOMOPOULOS AND C. M. LEE (*Surgery*, May, 1960) report three cases of pancreatic pseudocysts in children under eight years of age and state that this brings the total reported in the literature at this age group to 11. They think there is a possible causal relationship between the pancreatitis of mumps and some cases of pancreatic pseudocysts in young children. They point out also that spontaneous non-specific pancreatitis also occurs occasionally in this age group and may result in pseudocyst formation. However, the usual cause of this lesion in childhood is blunt abdominal trauma. The authors consider that many unreported cases occur and state that the incidence will increase with the rising rate of motor accidents and other sources of abdominal injury. They point out that treatment is more or less the same as for an adult. They consider that it is easier to dissect out the cysts in young children than in the adults, but that in most instances marsupialization is the safest procedure. Its disadvantage is that drainage is sometimes protracted. The authors conclude that pancreatic pseudocysts are not actually very uncommon as a childhood disorder, and suggest that they should occupy a more prominent place than they do at the moment in the diagnostic consideration of abdominal masses in childhood.

Ischæmia of the Colon Complicating Operations on the Aorta.

R. F. SMITH AND D. E. SZILAGYI (*A.M.A. Arch. Surg.*, May, 1960) state that during abdominal aortic aneurysmectomy technical necessities require the sacrifice of the inferior mesenteric artery and the temporary clamping of both internal iliac arteries, which means that there is a sudden temporary occlusion of the distal inflow arc of the sigmoid and superior hæmorrhoidal arterial communications. If these communications are normal the proximal inflow arc will supply enough blood to ensure viability of the bowel while the distal arc is temporarily interrupted. However, in about 10% of cases this temporary stoppage of the distal inflow leads to ischæmia severe enough to cause necrosis of the mucosa or of the deeper layers of the recto-sigmoid portion of the colon. Interruption of this primary collateral arterial circuit of sudden onset and prolonged or permanent interruption will invariably result in severe bowel ischæmia. When the obliteration of the inferior mesenteric artery or of the two internal iliac arteries, or of both, takes place gradually, secondary collateral arterial pathways are established and ischæmia of the left side of the colon usually does not occur. After aneurysmectomy of the abdominal part of the aorta, care must be taken to reestablish the continuity of blood flow in at least one internal iliac artery, and the blood supply of the left half of the colon, especially of the recto-sigmoid area, must be carefully observed during the operation. In the early stages after such operations, distension, diarrhœa or melæna may be a manifestation of ischæmic changes of the recto-sigmoid region, and this will require a diverting colostomy. Compromise of the blood supply of the left half of the colon by the complications of atherosclerotic lesions of the aorta may lead to clinical manifestations that appear colonic in origin, such as acute ulcerative colitis secondary to impairment of the colonic blood supply by an expanding aneurysm. Two instances of fatal colonic ischæmia complicating aortic operations are described. One was caused by ligation of an anomalous communicating arterial branch of critical importance and another was caused by multiple atherosclerotic arterial emboli.

Elective Neck Dissection for Intraoral Cancer.

H. W. SOUTHWICK *et alii* (*A.M.A. Arch. Surg.*, June, 1960) review the findings associated with 192 head and neck operations for intraoral cancer. They found microscopic evidence of metastatic disease in 50% of the cases. Clinically negative lymph nodes were microscopically negative in 40% of cases. The authors found no evidence of primary contralateral metastases. They consider that a regional node dissection should be performed for primary tumours of the tongue and floor of the mouth when the patient's general state of health does not contraindicate such an operation.

Surgical Management of Parotid Lesions.

O. H. BEAHRS *et alii* (*A.M.A. Arch. Surg.*, June, 1960) present a study of 760 surgically treated patients with parotid lesions seen at the Mayo Clinic from 1945 to 1954. Of these lesions, 79% were benign and 21% were malignant. The ten-year recurrence rate of mixed tumours treated by enucleation or excision was 10% for primary lesions and 31% for recurrent lesions. None of the 47 patients treated by conservative parotidectomy for primary mixed tumours and observed for three to five years had a single recurrence. Recurrence within three years occurred in 35% of the patients with moderately malignant lesions and 73% of those with highly malignant lesions. The five-year survival rate of patients with moderately malignant tumours varied from 76% to 92%; for patients with highly malignant tumours, it ranged from 31% to 57%. The authors advocate subtotal or total conservative parotidectomy for most benign lesions of the parotid gland, with total radical parotidectomy for malignant lesions.

Cavernous Transformation of the Portal Vein.

L. LOGER AND P. E. B. HOLMES (*Brit. J. Surg.*, September, 1960) present the case histories of four patients with cavernous transformation of the portal vein. Their ages were 35 years, 37 years, 39 years and 15 years. These patients exhibited the signs and symptoms of portal hypertension and hypersplenism. Spleno-portography and splenomanometry, when these tests are possible, are of great value in establishing the diagnosis and the site of the obstruction. The cause of cavernous changes in the portal vein is debatable, but the authors consider that it is the end result of portal vein obstruction. The causes of portal vein thrombosis are listed as follows: (*a*) compression from without; (*b*) slowing of the portal circulation, due either to general disease such as heart failure, or to local conditions such as cirrhosis and congenital stricture of the portal vein; (*c*) diseases of the vein wall including phlebo-sclerosis, reaction to trauma, pylephlebitis and spreading thrombosis either neonatal or post-splenectomy; and (*d*) diseases of the blood such as polycythæmia. The treatment by means of shunt operations or palliative measures is discussed.

Primary Repair of Compound Skull Fractures in Children.

K. W. CARRINGTON *et alii* (*Surg., Gynec. Obstet.*, February, 1960) report on 20 children with compound skull fractures treated by replacing the free bone fragments as a primary procedure in 19, and by primary acrylic cranioplasty in one patient. The dural lacerations were closed primarily or with dural grafts. The authors conclude that the use of free bone fragments had resulted in primary healing in all, without the development of pulsatile skull or other complications. They believe that the incidence of post-traumatic epilepsy may have been reduced by this procedure and that the parents have been relieved of considerable anxiety and the patients of a source of potential danger.

Heller's Operation for Cardiospasm.

K. DOUGLAS AND F. NICHOLSON (*Brit. J. Surg.*, November, 1959) state that since Willis described cardiospasm in 1672 its treatment has been empirical, for, in spite of many theories, nothing is definitely known of its ætiology. They have studied 42 cases of cardiospasm

over an eight-year period; of the patients in this series, 28 were submitted to a Heller operation. In 11 patients the result was excellent, and in 8 patients the result is described as satisfactory. The causes of failure and the technique of Heller's operation, with slight modification, are discussed. The authors warn that reflux œsophagitis may complicate an otherwise excellent result.

Zollinger-Ellison Syndrome.

W. I. CAWKWELL (*N.Z. Med. J.*, October, 1960) states that since Zollinger and Ellison in 1955 reported two cases of primary non-specific jejunal ulcers associated with marked gastric hypersecretion and hyperacidity and found non-specific islet-cell tumours of the pancreas in each case, this combination of findings has come to be widely known as the Zollinger-Ellison syndrome and many more cases have been reported. The author adds a further case of his own, which he believes to be the first to be reported from New Zealand. The patient in this case was 11 years old when first investigated, and is the youngest reported in any of the available literature on this condition. After three laparotomies and a stormy history of hæmatemesis, melæna and jejunal ulceration, the condition was recognized as a case of the Zollinger-Ellison syndrome, and at a fourth laparotomy a partial pancreatectomy was performed. Histological examination showed no evidence of a tumour, but there was diffuse hyperplasia of the islet tissue involving the alpha cells throughout the gland. The patient made a good recovery and still remained free of her previous symptoms a year after the final operation.

Treatment of Second-Degree Burns with Amniotic Membrane.

J. PIGEON (*Canad. med. Ass. J.*, October 15, 1960) discusses the use of amniotic membrane in the treatment of second-degree burns, and describes nine illustrative cases. He states that ideally the injured tissue should be replaced by healthy epidermis. Homografts are at present the subject of intensive study and experiment, but their present development is still far from offering a readily available dressing in quantity. The amnion, formed by the ectoderm of the fœtus, is the nearest thing to the epidermis; it is extremely elastic and more easily manipulated than a thin skin graft; its application to denuded dermis stops pain immediately and prevents fluid loss. The author suggests that the fear of transmitting infection has prevented the general acceptance of amnion as a dressing, and that as blood transfusion never became practical on a large scale until means were found to preserve and bank blood, so the use of amniotic membrane should gain general acceptance if we have a technique of preparation and preservation that makes it safe, simple and effective. He describes the technique used at Blind River. In vaginal deliveries a sterile towel is used to receive the afterbirth, contamination with blood being avoided as much as possible. The amniotic membrane is then peeled off the chorion, cleaned in a 1 : 1000 solution of "Cetavlon" and then transferred to a sterile jar containing one part "Zephiran" in 10,000 of saline. This is kept in a blood-bank refrigerator and periodically checked for sterility. These membranes remain sterile for months. There is no evidence that the amniotic tissue reproduces on the skin, but it seems to undergo the same type of change as the cornified cells of the epidermis, and when a dressing is removed after 10 to 15 days, the membrane is dry and hard, like thin transparent plastic material. The application of the membrane to the burnt surface is simple, and no anæsthetic is required. Strict aseptic technique is extremely desirable. After the membrane has been applied, it is covered with petrolatum gauze and a gauze pad, immobilized by compressive bandages where possible. Antibiotics are administered only if complications threaten. The dressing is not changed for from 10 to 15 days. The method loses its superiority if third degree burns are present, and is not suitable if infection is already present. The author concludes by stating that in his experience this form of treatment of second-degree burns has proved the most effective and practical method.

Primary Duodenal Diverticula.

D. LANE (*Aust. N.Z. J. Surg.*, August, 1960) reviews a series of cases of duodenal diverticulum in which the patient had been admitted to hospital in Brisbane. In eight of these cases operations for excision of the diverticulum were performed; one patient died as a result of pancreatitis. The author describes five cases from his own records to illustrate some of the problems of duodenal diverticula, and points out that there are many pitfalls involved in both diagnosis and treatment of the condition; he notes that the incidence of bleeding in this series was surprisingly high. He states that it is difficult to ascertain the effect of excisions of the uncomplicated diverticulum, and quotes a report from the Mayo Clinic which indicates that definite benefit from operation can be expected in only about 50% of the most carefully selected patients. He notes that many of the patients proved very vague in their symptomatology and that cases for operation must be selected with great care. Many barium meals may be required to establish the correct diagnosis. The author states that cholecystectomy was performed much too readily in this series, and stresses that this should be done only if the gall-bladder is the seat of some pathological process. In discussing the difficulties and dangers of operation, he states that the chief danger is pancreatitis, which may arise even if the pancreas has been minimally handled. If at operation the diverticulum is found to be embedded in the pancreas and possesses a wide mouth, the author suggests that it is probably better to leave it alone. In conclusion, he states that operations on duodenal diverticulitis are rarely justified unless complications arise, and that it is important to assess not only the type of diverticulum but also the type of patient in whom it is found.

Brachial Plexus Analgesia.

B. J. POLLARD (*Aust. N.Z. J. Surg.*, November, 1960) discusses the technique and indications for brachial plexus analgesia. He states that this technique has undergone marked fluctuations in popularity, but that in recent years it has taken its place with other methods in the anæsthetist's repertoire, with its own indications and unique advantages. After a brief historical note, the author outlines the anatomical considerations and then describes the procedure in some detail. In discussing the indications for brachial plexus analgesia, he states that it is eminently unsuitable for out-patient procedures of some severity, particularly in accident cases in which the patient is not prepared for general anæsthesia, but that it is not worth the time and effort for minor conditions, where a simpler method will suffice. In the aged, the risk of local analgesia may be less than that of general anæsthesia. The vasodilatation produced by the block may be advantageous in certain cases. A tourniquet can be used if needed, but this should be done with caution. The author states that for plastic surgery on the upper limb, brachial analgesia comes nearest to filling an ideal role; with acute injuries there need be no delay in treatment, and almost no patient need be rejected on the ground of unsuitability. Finally, the author states that in his opinion brachial block is a luxury form of anæsthesia and should be performed only by those who have learned the method under supervision. He quotes an earlier writer to the effect that the supraclavicular method of brachial plexus block eliminates pain from the arm, forearm and hand and produces a motor and sensory paralysis directly proportionate to the degree of skill with which the anæsthesia has been produced.

Anterior Tibial Artery Occlusion.

B. VENNER (*Aust. N.Z. J. Surg.*, November, 1960), in discussing anterior tibial artery occlusion and related syndromes, states that though the manifestations of peripheral vascular disease are commonplace, involvement of the anterior tibial artery has not received much attention in the past. Acute occlusion of this vessel produces a characteristic syndrome, but one which may cause some confusion. There occurs an acute ischæmia, not of the whole limb, but of the anterior tibial compartment and the overlying skin, and the result may vary from massive gangrene of the region, through fibrous contracture to complete recovery. The author describes a case of occlusion due to embolism, in which gangrene of the tissues of the anterior tibial compartment occurred, resulting ultimately in amputation. The related condition of the anterior tibial syndrome is also discussed and two cases are described; in this, ischæmia of the muscles of the anterior tibial compartment occurs without vascular occlusion, and the exact ætiology is obscure; it may occur after unaccustomed exertion. The author states that early recognition of the anterior tibial syndrome is necessary, so that division of the deep fascia of the compartment may be performed in the hope of mitigating the effects of the ischæmia. Occlusion of the anterior tibial artery and the anterior tibial artery syndrome may, under certain circumstances, be confused with lesions directly due to trauma or with acute inflammatory lesions.

The Wider View.

A PHYSICIAN IN THE CONGO, 1960.

AMONG the far-reaching effects of the crisis which occurred in the Republic of the Congo soon after its birth in July last year, not the least was the threatened breakdown of its health services. To meet this emergency, at the request of the United Nations Organization, the International Committee of the Red Cross and the League of Red Cross Societies organized a joint operation to provide medical assistance. As its contribution, the Australian Red Cross Society provided two medical teams, each comprising a surgeon, a physician and a male nurse.

The extent and nature of the problems which arose can be appreciated by considering the situations before and after independence in the medical field. Under the Belgian system the health services, both on the curative and on the preventive sides, were highly developed and organized. While government services played the major role, there were, in addition, a number of non-governmental health agencies, such as medical foundations of the Belgian Universities, Red Cross and missionary medical bodies, subsidized and supervised by the Government. As well, there were private medical services consisting of private practitioners and the organizations of private societies and industrial concerns. Medical care for the population of nearly fourteen million people was provided by a series of establishments, including hospitals, both urban and rural, an extensive network of out-patient clinics and health centres, as well as by mobile medical teams. The bed-to-population ratio in the country towards the end of 1959 was 6·2 per 1000, and the total expenditure for medical services in that year was about fifty-five million U.S. dollars or nearly four dollars per head.

The key to an understanding of the partial collapse of the health services is found if figures relating to the numbers of medical workers in the Belgian Congo towards the end of its days are examined. The following categories and numbers of personnel existed in the country in December, 1959, that is, six months before independence:

Medical Personnel.

Doctors	761
Pharmacists	75
Dentists	44
Biologists	11
Assistants-médicaux	136

Paramedical Personnel.

European nurses	1223
Congolese trained nurses	1001
Nurse midwives	25
Nursing aides	3852
Midwives aides	466

Public Health Personnel.

(Doctors)	
Sanitary agents	623
Sanitarians	112

All the doctors, pharmacists, dentists and biologists (bacteriologists, entomologists, parasitologists, etc.) were Europeans, as were the midwives and over 50% of the trained nurses. On the public health side all the sanitary agents, who comprised two thirds of the total personnel, were Europeans. They were lay persons who had undergone a course of training at a school of tropical medicine, either in the Congo or in Belgium, and worked under the direction of the doctors (*hygiènistes*) in the service.

The *assistants-médicaux*, trained nurses and nursing aides and sanitarians made up the Congolese medical personnel. The category *assistant-médicaux* was specific to the Belgian Congo. They were trained in special schools, the educational requirements being four years of secondary education (ten years of schooling). The course consisted of four years of theoretical training and two years of practical work under the direct supervision of a doctor. After this they were required to do three years of internship in a recognized institution. They were not allowed private practice, and were committed to working for the Government or for a recognized non-governmental agency as assistants in hospitals, dispensaries or other medical units. The trained nurses were almost all males. After a primary education they received three years of training in a school for nurses. Many of them were not utilized for nursing duties but acted as laboratory technicians or administrators, or were placed at the head of small medical establishments. The educational level of the nursing aides was very low and in many instances they were illiterate. They were given two years of practical training. For the sanitarian, the diploma of a graduate nurse was required and in addition a six-months course of training in the speciality. He worked under the direction of the European sanitary agent.

Responsible as the Europeans were for its direction, and filling all key specialities in the medical service for which there were no trained Congolese equivalents, the consequences of the exodus of Europeans which occurred were serious in the extreme. The number who left the country is not accurately known. That it was large can be appreciated by the fact that as an initial project the World Health Organization undertook to engage a group comprising 130 doctors, laboratory technicians, sanitary engineers, bacteriologists and other categories, its ultimate aim being between four and five hundred such personnel. Also, most of the hospitals were still seriously short of doctors, and many had none at all, when members of Red Cross and Red Crescent teams and medical teams sent by Governments reached a peak of 160 towards the end of last year. The nursing services were less severely affected, as, while there was a number of secular European nurses, the majority were religious sisters, many of whom remained in the country.

The Australian teams arrived in Leopoldville on August 22 last year. The Senior WHO Representative and the Chief Delegates of the International Red Cross Committee in the Congo, in cooperation with the Congolese Government, were responsible for assignments to regions requiring staff. For security reasons, the general policy adopted was to place Red Cross teams in areas occupied by U.N. troops. As this was a comparatively early stage in the U.N. operation, some banking up of medical personnel had occurred in the capital.

After a week in Leopoldville we were flown to Bakwanga in the southern part of the Kasai Province. The town lies about five hundred air miles to the east and is a mining centre. In normal times it was said to have produced nearly 75% of the world's industrial diamonds. Several hospitals in the area were now without skilled staff, and additional medical problems had been raised by an influx into it of between 200,000 and 300,000 Baluba refugees as a result of intertribal warfare.

Although the authorities in Leopoldville had not been aware of the fact, more recent complications had developed. Two or three days before our arrival a large number of the Congolese Force Publique had stormed the town, and fighting between them and the natives of the area was in progress. The situation had arisen because a local leader, Albert Kalongi, following the example of Katanga and with the support of the Baluba tribesmen of this region, had indicated his intentions of establishing the South Kasai as an independent State. The Lumumba Government had sent in its forces to suppress the movement. The normal activities of Bakwanga had come to a standstill. There were no Congolese civilians to be seen in the streets, and the mines had ceased to function. The remaining Belgian residents, 150 of them, had left their homes and collected in a large club at the centre of the town guarded by U.N. Tunisian troops.

A visit to the native hospital, which lay a few miles out of the town, provided a first encounter with the Force

Publique as, en route, it was necessary to pass through their guard posts. During the course of lengthy interrogations, with a Tunisian officer acting as interpreter, the soldiers were aggressive and suspicious. While the words "*Croix-Rouge*" produced a glimmer of understanding, "*Australie*" obviously conveyed nothing. Nevertheless, eventually permission was given to proceed. It was as well that the precaution of discarding caps and removing all insignia other than Red Cross badges had been taken beforehand, as a military type uniform, similar in appearance to that of the former Belgian officers, would have proved a decided disadvantage. At the hospital there seemed to be little immediate prospect of work. As the patients were Balubas, more than two-thirds of them had fled.

With the fighting in the town continuing, the situation remained confused until the positive move of approaching the Commandant of the Force Publique was made by the senior officers of the teams. In the negotiations which followed they were considerably assisted, as indeed was all our subsequent work in the South Kasai, by a member of the American Presbyterian Congo Mission Organization, with many years' experience of the country and its people, who volunteered his services as interpreter. When the neutrality of Red Cross was stressed and it was made clear to him that his sick and wounded would be treated as well as those of the opposing faction, the Congolese Commandant proved cooperative, guaranteeing no interference from his men, whom he instructed accordingly.

Although the Baluba people were putting up a fierce and determined resistance, their antiquated firearms, spears and arrows were no match for the mortars, machine guns, grenades and modern rifles of the Lumumba force, and many of the engagements which occurred amounted to little better than massacres. In one such episode 60 natives, probably all civilians, and including some women and children, were machine-gunned in school rooms behind the Catholic Mission, where they had taken refuge. One adult male and six infants in the nursery of a small attached maternity unit were the only survivors. The mass burial was undertaken by the team members with the assistance of some Belgian priests. Burial of the dead during the period in Bakwanga became a familiar duty.

As by now the number of wounded was mounting, work at the hospital commenced, the surgeons and medical orderlies being fully occupied. Although it was anticipated that trouble might arise, they were able with little difficulty to admit patients of both sides, and even the rule that no firearms were permitted in the building was respected. The town's three Belgian doctors also resumed their duties in the other departments of the hospital.

There were a variety of tasks elsewhere for the physicians. One task was to run a daily sick parade at the Force Publique camp, which paid dividends as far as personal relations were concerned. Collection of wounded and their transport to hospital also occupied a good deal of time. Frequently this entailed a house-to-house search in the otherwise deserted and burnt-out villages, as the casualties preferred to go into hiding rather than to run the risk of making their way to hospital. Often they had been lying seriously wounded for two or three days before being found.

Visits were made to outlying areas to investigate the hospital position and general health problems. A serious situation existed in one small town, approximately 20 miles to the south-west, in which there was a heavy concentration of refugees. There was a severe shortage of food in the area daily growing worse, and the 200-bed hospital, run by a medical assistant and some native nurses, was without water and electricity. In the crowded wards were a number of wounded requiring surgery, and smallpox had broken out among the children. Although it was considered that at a later date one of the teams might transfer to this centre, existing conditions were such as to make this impracticable. However, regular visits were made, diesel fuel necessary for the functioning of the water and electricity plant being carried, as well as food such as milk powder, flour and dried fish. Because of distance, limited transport facilities and shortage of manpower, these supplies were by no means adequate to meet the need. On return trips the wounded and some of the seriously ill were transferred to the Bakwanga hospital.

The country to the south-east, into which the fighting had moved from the town, appeared in direct contrast to the heavily peopled refugee areas. Along the roads and in the tall grass on either side lay numbers of dead, and for many miles village after village was partially destroyed and deserted. In one town a tuberculosis sanatorium, in which nearly 200 patients had been under treatment, had been looted and wrecked. On a search of the wards and isolation blocks only three wounded patients were found. A mission in the vicinity had received similar attention. Among those killed were several school children and the members of two complete families, who had been burnt to death in a hut.

While relations with the Government soldiery remained good, the Baluba villagers adopted a cautious and suspicious attitude towards us. When we were passing through their territory halts were made every few miles in an endeavour to establish friendly relations. Such overtures would not have been possible without the assistance and tact of our American interpreter. Even more difficult to deal with were the undisciplined guerilla groups occasionally encountered. In at least one locality acceptance by the natives suffered a temporary set back. This came about when the Red Cross truck ran into the fringes of a skirmish, and inadvertently, in sight of their enemies, supplied a means of evacuation for a number of reatreating Lumumba troops. Unfortunately, medical work in the South Kasai was considerably hampered by the conditions described, and much unfinished business remained when, by order of the Commanding Officer of the Tunisian force, the teams were transferred to Luluabourg, the capital of the Kasai Province. Here one team remained to work in the local native hospital, while the other moved to a centre some 150 miles to the south.

Luluabourg is a large and attractive town of wide boulevards and modern multistoried concrete buildings. After the events of July all but 54 of its former 3600 European inhabitants had left. Its native population are members of the Lulua tribe. In the months preceding independence, a fierce uprising of these people had taken place against the Balubas, who over the years had subtly infiltrated their territory and under the Belgians had held many of the best positions open to natives. As a result the Balubas were driven eastwards towards Bakwanga, and this gave rise to the refugee problem already mentioned.

The hospital for the Congolese at Luluabourg was large and of modern construction with a bed capacity of 600. All the Belgian doctors who had been in charge of its various departments had left. Towards the end of July a Norwegian Red Cross team consisting of surgeon, anæsthetist and two female nurses had taken over its surgical department. The only other doctor on the staff was a Spanish physician employed by the Congolese Government. When their term expired a few weeks after our arrival, the duties of the Norwegians were taken over by the surgeon of the Australian team, assisted by the medical orderly and a nursing nun who acted as anæsthetist. Later in the year a Belgian obstetrician and gynæcologist returned, bringing the medical staff up to four. On the nursing side were three Belgian trained nurses and three nuns who had remained at their posts. The rest of the staff were Congolese, the greater percentage of them only partially trained. All hospital administration positions were held by Congolese, most of them former trained or semi-trained nurses. The WHO adviser to the Congolese Minister of Health of the Province acted as a liaison officer between Red Cross personnel and administrative staff.

Since my own duties were concerned with the children's wards, these are discussed in more detail. However, an account of conditions here reflects to some extent those

which prevailed in other departments. When the Belgian pædiatrician relinquished office, her place was taken by a medical assistant. A few days after our advent he left to continue his studies abroad. In charge of the staff of Congolese nurses, most of whose training had halted at various levels, was a Belgian trained nurse. In a delicate position by virtue of her nationality, and in the face of many difficulties and frustrations, she had nevertheless succeeded in preventing much of the deterioration in discipline and of former standards apparent in some of the other sections.

Soon after work was commenced it was noticed that the number of patients was increasing daily. This was seen in all departments, and in time the numbers reached embarrassing proportions. There were in mid-September 80 child in-patients. By early January this figure had doubled. Since, in accordance with established custom, the patient was usually accompanied by its mother and her younger children, accommodation problems were considerable. The fact that the hospital had earlier been looted and most of the bed clothing and children's garments taken added to the difficulties. There were several possible explanations for the increase in hospital attendance. Immediately after the departure of the Belgian staff, numbers of both in-patients and out-patients had fallen considerably. Many of the people, conscious of the status of the Congolese medical personnel, were reluctant to consult them. Probably the stimulus for them again to seek attention was the reappearance of European doctors. In addition, most of the outlying areas were without skilled staff of any kind, and it was to be expected that in time the sick would gravitate to main centres. Though difficult to assess, the breakdown of preventive medical services was possibly also a contributory factor to the rising hospital population.

Among the children, the commonest condition encountered was protein malnutrition of varying degrees of severity, including many cases of frank kwashiorkor. This was given a certain amount of publicity in the Press, the implication being that it was a post-independence phenomenon. However, it had always been a problem in the Congo due to the traditional low protein diet of the people. Severe anæmia was very frequent. Besides that accompanying hookworm infestation, malaria and nutritional deficiencies, a high proportion of the cases was of the sickle cell variety. Of the parasitic diseases, due to relaxation of control measures, the incidence of malaria, high at any time, appeared to be on the increase. Hookworm and round worm were rife, and schistosomiasis was not uncommon. This was not an endemic area for trypanosomiasis. As might be expected, diseases due to poor sanitary standards, such as salmonella infections, the dysenteries and infectious hepatitis, were responsible for a large number of admissions. Approximately 15% of in-patients were suffering from tuberculosis. Towards the end of the year there was a marked increase in the number of cases of pyogenic meningitis. Bronchopneumonia, measles, whooping-cough and chicken-pox were ever present.

As far as general working conditions were concerned, there were a number of problems. One, which required prompt attention, was the language difficulty. It was necessary to spend quite some time brushing up our French, as a knowledge of it was essential, not only for hospital work, but in most other situations met with in daily life. By taking lessons also in Tshiluba, the native dialect of the area, a working knowledge was acquired sufficient to deal with the patients, most of whom were non-French speaking. Despite occasional independence-born truculence, "walk outs" and once an abortive move to get rid of all European staff, relations with the Congolese nursing and administration staff were cordial on the whole. The nurses, however, required constant supervision, and medical officers were often involved in ward tasks not normally demanded of them. There was a very well equipped laboratory, but owing to lack of trained technicians, only limited investigations could be done, and results were frequently unreliable. However, this service was valuable at least in the fields of bacteriology and hæmatology, and a blood bank was maintained, as two members of the former Belgian staff had remained. Unfortunately they left later in the year. Considerable inconvenience was caused a few weeks after our arrival by the breakdown of the main X-ray machine, which remained out of action as no one could be found to repair it. Though there were shortages of many items, making it necessary often to resort to second choice and unfamiliar therapy, the supply of life-saving drugs, such as antibiotics and anti-malarials, was adequate to meet demands.

So much for the present; what of the future? The first two Congolese doctors are expected to graduate this year from the Lovanium University in Leopoldville, which, it is possible, may have produced 19 by 1965. Studying under WHO fellowships at medical schools mainly in France are 60 of the former *assistants-médicaux* and seven other selected candidates. Meanwhile, now in its eighth month, the Red Cross medical action continues. The original teams, recruited from over 20 countries, have been replaced by new ones and, in conjunction with an increasing number of WHO workers, are maintaining the health services of the Congo.

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Out of the Past.

POWDERED MILK.[1]

[From the *Australasian Medical Gazette*, April 21, 1902.]

ACCORDING to a recent consular report, Dr. Ekenberg, of Gothenberg, has worked out a method of reducing milk to the form of powder, which will be of far-reaching importance to the business of dairy farming. It is said that the product possesses all the qualities of milk in concentrated form, except that moisture is absent, and that it will not get sour or ferment. The milk flour is completely soluble in water, and can easily be transported in tins, barrels or bags.

British Medical Association.

RADIOLOGICAL AND PATHOLOGICAL REPORTS ON REPATRIATION PATIENTS.

THE following letter from the Acting Chairman of the Repatriation Commission is published at the request of the General Secretary of the Federal Council. It concerns radiological and pathological reports on repatriation patients and is the reply to representations made by the Federal Council subsequently to its meeting of September 26, 1959.

Repatriation Department,
1st March, 1961.

Dear Dr. Hunter,

The representations of the Federal Council of the British Medical Association as set out in your letter 7548 of 16th October, 1959, have now been fully considered by the Repatriation Commission.

2. The Commission has decided that Local Medical Officers in country areas need not in future seek prior approval from the Department before arranging consultations, radiological and pathological examinations provided that:

(*a*) the consultation, etc. is necessary for treatment of a disability which the patient's Entitlement Card shows to be a departmental responsibility;

(*b*) Commonwealth facilities, if available, or the services of a medical practitioner who has agreed to examine patients for the Department at prescribed or arranged fees are used (a list of local facilities and the names of these medical practitioners is to be supplied to the Local Medical Officer on request); and

[1] From the original in the Mitchell Library, Sydney.

(c) notification of the consultation, etc., is forwarded by the Local Medical Officer to the Department as soon as possible.

3. It will be necessary for Local Medical Officers to adhere strictly to these requirements, which are a prerequisite for payment of fees by the Department for such services.

4. If a Local Medical Officer is uncertain whether a particular consultation, etc., is a Departmental responsibility, we suggest that he refer to the Department, unless the case is one of extreme urgency. A trunk-line call, which may be charged to the Department, will elicit prompt advice.

5. Appropriate advice will be forwarded to all Local Medical Officers in country areas as soon as possible. I would also be pleased if your Association would give the matter suitable publicity in its circulars to members.

(Sgd.) A. L. GOULD,
Acting Chairman,
Repatriation Commission.

Dr. J. G. Hunter,
General Secretary, Federal Council.

A LETTER OF APPRECIATION.

THE following letter from Dr. S. WAND, Chairman of Council of the British Medical Association, is published at the request of the General Secretary of the Federal Council. It was written to the President of the Federal Council, Dr. H. C. Colville, on the eve of Dr. Wand's departure from Australia.

February 26, 1961.

Dear Cecil,

Today we have been to Canberra and it is with much regret that we realise that this is our last port of call in Australia. Throughout our necessarily rather hurried tour we have received the most wonderful hospitality. We have been wined, dined and feted. We have been shown many of the wonders of Australia. We have stayed at sumptuous hotels as your guests. Doctors and their wives have given us unstintingly of their time and no wish of ours has gone unfulfilled. Everything has been done to minimise the inconveniences of travel.

When we return we shall report on the wonders and development we have seen and the dignity and initiative of the Australian people.

I hope you will express our thanks to the doctors of Australia. I feel that we have a very close affinity and I know that I speak for all my colleagues at home when I say that, whatever developments may be necessary in the future, we for our part desire the closest possible bond—a bond that is certainly not weakened by the distance between us.

Please convey my particular thanks to John Hunter and accept them for yourself.

With all good wishes,

Yours sincerely,
(Sgd.) S. WAND.

Correspondence.

MEDICAL CERTIFICATES.

SIR: Because of bad organization, the giving of medical certificates is not at all satisfactory. The commonest irregularity is the giving of a medical certificate after the patient has recovered and was not examined during the illness. A request for a certificate is often made after an attack of influenza or other illness, when the patient is informed by his employer that he will not receive sick pay unless he produces a medical certificate. Every practitioner has been faced with this problem.

Hoping to improve the situation, the Medical Board of Victoria issued a dire threat in a memorandum sent to all registered medical practitioners. Warnings are sent out by the Board periodically. We have been told that "the issue of misleading certificates may constitute misconduct sufficiently serious to warrant erasure from the Medical Register".

I suggest that the issuing of such threats is unnecessary and shows a misunderstanding of the situation. Neither the doctor nor the patient is to blame. The fault lies with the employer. Workers, especially "New Australians", have a right to know what is required of them. The Chamber of Manufactures and other employers' organizations should be advised to display prominently in all workshops and other places of employment the following notice:

Absence from Work Because of Illness.

When an employee is absent from work for more than one day because of illness a Medical Certificate is required by the Management. It is not sufficient that the doctor be asked to give you a Certificate when you have completely recovered from the illness. We cannot be expected to accept such a certificate. Your doctor should see you when you actually become ill. With his help you should recover sooner. If you remember this there will be no dispute about your doctor's certificate and we will all be saved much inconvenience.

It is probable that the Medical Boards in other Australian States have encountered trouble with medical certificates. I offer the above suggestion as the best way of diminishing the number of unacceptable certificates.

Yours, etc.,

568 Neerim Road,
Hughesdale,
Victoria.
March 8, 1961.

VICTOR H. WALLACE.

THE NURSE IN SOCIAL MEDICINE.

SIR: Your editorial of January 28, 1961, was a welcome tribute to the nursing profession and to the health visitor in particular, and we are in complete agreement with your comments in relation to the importance of the public health nurse.

In view of the vital importance of the public health nurse in the community, whether she be a general health visitor or a specialist, this College has established a course in public health nursing, to commence in June, 1961, and to last six months on a full-time basis.

There is need for financial assistance to nurses undertaking this course, as has been done for other post-graduate courses, and it is hoped that employers of nurses who are doing public health work—for example, maternal and child welfare, pre-school and school nursing, industrial nursing and domiciliary nursing—will make scholarships available.

Yours, etc.,

G. N. BURBIDGE,
O.B.E., D.N. (London), F.C.N.A.,
President.

College of Nursing, Australia,
431 St. Kilda Road,
Melbourne, S.C.2.
March 9, 1961.

CARCINOMA OF THE BREAST: AN INTRODUCTION TO THE McWHIRTER CONTROVERSY.

SIR: I would like to present my views regarding these articles (MED. J. AUST., February 25, 1961) and hope they may be of interest to you and others. Regarding the article "Carcinoma of the Breast", the introductory paragraph of this article states that its object "is to review the general picture of management of carcinoma of the breast as managed in this State".

Unfortunately, amongst the "conclusions" reached at the end efforts are made to influence others in the treatment of carcinoma of the breast, and in my opinion their review and statistics should do no such thing. I personally am tired of the multiplicity of similar review articles which contain nothing more in effect than what has happened to patients with carcinoma of the breast in any one or group of institutions' or individual(s)' care. To attempt to use such a series to influence others is, I feel, misguided and undesirable, particularly as I can find no mention made

of the vital detail which in any one patient governs her personal survival — that is, the natural history and/or pathology of her individual tumour. Confronted by patients with similar tumours and clinical syndromes arising therefrom and dissimilar survival from treatment ordered as applicable to all Stage I (or II or whatever it is), one cannot condemn too strongly this terrible method of deciding so easily the stage (and therefore the assumed desired response) and prescribing a fixed course of treatment dependent upon the symbol arrived at.

It is this shallow and thoughtless process which is entirely responsible for the present chaos and reams of indeterminate literature regarding what is really a simple problem. It is not the survivors, but the patients who die, who lead one to the facts of mismanagement, and the sooner the pathologists are given their due share in management from the outset, the sooner we shall make real progress.

When will people treating cancer in general and carcinoma of the breast in particular realize that the type of tumour governs the survival and not much else does so? A "bad" cancer of the breast can be seen as "Stage I" and treated and soon dead, and whoever treated this can never attempt to improve his dire result until he knows the natural history of what he is tackling before cutting it up or in any other way interfering. The individual natural history of the individual patient's tumour can be sometimes guessed from the history. To cut the breast off and learn the natural history over the years, as is so widely done now, is a tedious business and of no help to the unfortunate patient; but we can learn fairly accurately the desired facts by a simple manœuvre — a biopsy performed at the patient's first attendance. The biopsy is essential, and unless undue delay occurs between this and definitive treatment, causes no harm except in a few rare and exceptional tumours. Any competent pathologist will verify the diagnosis and grade the tumour histologically, and in my experience are far more accurate in prognosticating the type of tumour present than the majority of clinicians give them credit for.

Armed with this vital and essential information, one is in a position to assess the primary and spread clinically, and then arrive at an optimum plan of attack regarding surgery, therapy, hormones, etc. The uselessness of the old International Staging is preevident by the writers here needing to split the stages up into groups, etc. Why use it if it will not encompass your wants? The tumour itself and each secondary each require to be assessed on criteria of operability, etc., and the only classification which allows this, of any real value, is the T.N.M. one, which is applicable to all tumours—the staging appropriate to the primary tumour ($T_1 \rightarrow T_4$), local or regional nodes ($N_0 N_1$, etc.) and metastases (M)—will automatically give a comprehensive written statement embracing all factors of surgical interest and importance.

The third essential to correctly govern treatment is the correct appreciation of what radiotherapy can or tries to do. This must be realized at the outset, or it will often either be rendered ineffective or undesirable in any individual patient. I bring this matter up to correct the loose and useless statement made under paragraph 9, page 287—"Stage II (other than early Stage II) patients would appear to be best treated by simple mastectomy and full post-operative irradiation". As a generalization it may contain truth, but it is grossly inadequate as it stands.

It is utterly undesirable to treat all "Stage II (other than early Stage II)" the same, because it is not until appreciation of radiotherapeutic possibilities has reached the conscious level and its use in the correct place and sequence is routine that we can hope to even slightly progress by improving results. The response of a tumour to radiation is not usually obviously related to gross histology, and it is thus not sound practice to irradiate indiscriminately all anaplastic grade III cancers of the breast. What is essential is to irradiate preoperatively all anaplastic tumours (operable according to their T.N.M. criteria, of course), because the patients with these tumours die of metastases, and although irradiation can control to a certain extent some of these tumours, its role is primarily to help sterilize the continual flood of blood-borne metastatic cells and is given for this purpose alone. I have practised therapy for too many years to have sufficient faith in it alone for me to suggest other than that the primary is removed at the optimum time by any suitable operation. The optimum time of "no trouble" is arrived at by a simple appreciation of the post-radiational endarteritis that occurs locally, and operative healing must be ahead of this process. The grade III cases which were "inoperable" at the start according to their T.N.M. staging can have post-radiationally any required surgical manœuvre to suit the individual patient—for example, excision of an indolent primary mass. Grade II cases probably require similar handling.

The low-grade tumours (Grade I) of course do not usually metastasize (a few do), but if operable on T.N.M. classification then there is little justification for preoperative radiation, and so proceed to a radical mastectomy at once. It is in this group alone (about 15% of operable cases) that it may be justified to do more extensive excisional procedures. I say radical, because it should be curative, whereas a simple mastectomy could not be guaranteed such in spite of post-operative irradiation. If the pathologists report that the axillary nodes are uninvaded histologically, then in an outer quadrant tumour post-operative radiation is a sheer waste of time, machine time and money. Indeed, the morbidity of radiation may actually lessen the survivals when it is used. An inner quadrant or central low-grade tumour treated by radical mastectomy does not have its nearest adjacent nodes removed, and here is the value of post-operative therapy; it is used to destroy residual tumour locally, and when it is used it is because such tumour residue probably does exist, and one assumes that probably the internal mammary nodes contain it when inner quadrant tumours are present. Post-operative therapy is also indicated if there is any reason to suspect malignant cells remaining in the scar and chest wall, and also to the remains of axilla and supraclavicular region if the nodes were invaded pathologically. It must be clearly understood that as soon as post-operative radiation is indicated in the above scheme, it is tantamount to admitting that the cases treated are pretty certainly inadequately treated by their surgery alone, and survival may depend upon the excellence or otherwise of the therapy.

Low-grade inoperable (on T.N.M. basis) tumours require radiation with or without later surgery as indicated, and it is in this group that therapy is of greatest value, because these patients live for years and years with local slow spread and therapy may even eradicate the disease.

I deal with these points in greater detail than demanded in the inherent nature of my criticism of this article, but for the reason that it is only by a very careful appreciation of these points and their correct application to any one individual that we can see the wood for the trees in treating cancer of the breast.

The second article I noted regarding the McWhirter controversy is the main reason for this detail, as I am tired also of reading the literature of the protagonists who, I feel, are arguing over individual preferences of treatment, none of which appears rational to me, as it neglects the very basic characters of the disease which I have attempted to outline. In the treatment of any one individual patient for optimum survival, the treatment must depend on the correct sequential integration of radiotherapy, surgery, hormones as indicated by the type of tumour and natural history in that individual. All combinations of treatment have their true place, and the continued argument between groups who favour certain combinations merely indicates that either the group has no real grasp of the problem, or that it has treated patients with insufficient information to justify its policy in any individual patient.

Yours, etc.,

JOHN A. G. HOLT,
M.B., Ch.B., F.R.C.S., F.F.R., M.C.R.A.,
Medical Director.

Institute of Radiotherapy,
Western Australia.
March 5, 1961.

BOOKS AND BOOK REVIEWS.

SIR: In the editorial of the fourth instant you call for comment about the book reviews in your Journal. The policy of anonymity of reviewers, favoured by Editors of THE MEDICAL JOURNAL OF AUSTRALIA, had never seemed quite fair to me. Recently my views were transformed by reading in *The Times Literary Supplement* of January 13, 1961, T. S. Eliot's tribute to Sir Bruce Richmond, editor of this distinguished publication from 1902 until 1937, on the occasion of Sir Bruce's ninetieth birthday. In acknowledging his debt to him, Eliot writes, *inter alia*:

> One lesson that I learnt from writing for *The Times Literary Supplement* under Richmond was that of the discipline of anonymity. I had served my apprenticeship as a reviewer in *The Athenaeum* under Murry, but there all the articles and reviews were signed. I am firmly convinced that every young literary critic should

learn to write for some periodical in which his contributions will be anonymous. Richmond did not hesitate to object or delete, and I had always to admit that he was right. I learnt to moderate my dislikes and crotchets, to write in a temperate and impartial way; I learnt that some things are permissible when they appear over one's name, which become tasteless eccentricity or unseemly violence when unsigned. The writer of the anonymous article or review must subdue himself to his editor—but the editor must be a man to whom the writer can subdue himself and preserve his self-respect. It is also necessary that the editor should read every word of what he prints; for he is much more deeply inculpated in what he prints anonymously, than in what he prints over the writer's name.

Needless to say, I beg to remain,

Sydney. ANONYMOUS.
March 13, 1961.

Obituary.

MALCOLM WELD FLETCHER.

WE are indebted by DR. JOHN H. COLEBATCH for the following additional contribution to the obituary notices of the late Dr. M. W. Fletcher.

Malcolm Fletcher's untimely passing last year in his adopted city of Launceston left many people, medical and lay, with a very deep sense of loss. Glowing, well-earned tributes to him, both as a physician and as a man, have already filled several columns of the obituary pages of this Journal. His unique personal qualities resulted amongst other things in his election, barely eight years after his arrival in Launceston, as chairman of the Northern Division of the Tasmanian Branch of the British Medical Association, and not long afterwards in his promotion to the position of president of the Tasmanian Branch. Many mainlanders recall with deep gratitude the kindness and the gracious hospitality of the President and his wife, Janet, during the Australasian Medical Congress in Hobart. Even more impressive, as witness to Malcolm's extraordinary influence on the community that he had served for only fourteen years, were the large congregation at the funeral service in St. John's Church, Launceston, and the very long rows of sisters and nurses from several hospitals who lined the streets outside. It must be seldom indeed that a doctor, whose professional life in Australia covered less than twenty years and ended at the age of fifty, has been accorded such demonstrations of admiration, esteem and affection.

Men of Malcolm's age are not often moved to submit obituary contributions for publication. My reason for doing so at this rather late stage is to ensure the placing on record of a few of the tributes that have been verbally expressed in recent months by his contemporaries from the Adelaide Medical School.

In his student days Malcolm was a versatile enthusiast, gaining first or second place in most of his examinations, being a year representative, taking a leading part in a wide range of faculty, college and other university activities, and participating in a variety of sports, in which he made up by tenacious efforts for any lack of ability. He was appreciated by his fellow-students for the same attributes that have already been mentioned by his Tasmanian colleagues of later years—"great kindness", "a genius for friendship", "sincerity", "forthrightness", "tenacity", etc. In addition to these we remember with affection his most generous nature, his absolute integrity, his capacity for self-criticism and his humility in spite of popularity and scholastic success. Conscientiousness sometimes made his responsibilities weigh rather heavily on his shoulders, particularly where patients were concerned; but this was balanced by an excellent sense of humour. At times he could be very outspoken and might argue heatedly, and yet, as a fellow student remarked recently, "he could not make an enemy" because there was never a hint of animosity towards his opponents. He had the gentleman's gift of being able to disagree without being disagreeable.

Malcolm had a wonderful partner and helpmate in his wife, Janet, who would not wish me to say more. Those fellow students who were fortunate enough to remain closely associated with him in later years share her delight in seeing his estimable and endearing qualities already appearing in their children. His achievements as described by the Tasmanian contributors indicate how well the early promise of his student days was fulfilled in the limited time he was with us. Apart from its brevity, Malcolm's life was in every sense a good life.

JOHN ROSS.

WE are indebted to DR. F. C. FLORANCE for the following account of the career of the late Dr. John Ross.

Last January, at the age of 73 years, Dr. John Ross died. He had been in practice in Chatswood from 1928 till 1960. His was a lovable nature, kindly, humorous, generous, wise, and he was revered by many of his patients whom he had attended over the years. He was a Scot, and the burr of his native Aberdeenshire never completely left him. Graduating from Mareschal College, University of Aberdeen, in 1911, he came to Australia from Glenkindie before World War I, and began practice in Queensland. At the outbreak of war, he returned to the United Kingdom and joined the Royal Army Medical Corps, and saw service in Salonika and France and finally became a prisoner of war towards the end of the war.

As the Sydney *Bulletin* so aptly put in its obituary notice, "King George V pinned on his Military Cross, awarded for staying behind with the wounded" during a break-through by the enemy. He returned to Herberton in the Atherton Tablelands after World War I, and resumed practice there till 1927, when he and his wife paid a visit to their homeland.

John Ross was a man of great courage, which showed up during four major operations due to a growth on his thigh over the last few years. No one ever heard him complain, and although sitting down and getting into his car for his daily rounds was always an ordeal, he carried on his practice as soon as possible after each operation. His limp became more and more obvious, and his last years were full of pain.

. . . . a behaviour so noble,
As gives a majesty to adversity.

To his widow, his beloved companion of many years, we offer our deepest sympathy.

Post-Graduate Work.

THE MELBOURNE MEDICAL POST-GRADUATE COMMITTEE.

PROGRAMME FOR APRIL, 1961.

THE Melbourne Medical Post-Graduate Committee announces the following programme for April, 1961.

Refresher Course in Medicine and Surgery.

From April 17 to 21, the honorary medical staff at the Royal Melbourne Hospital will conduct a refresher course in medicine and surgery suitable for general practitioners. The course will consist briefly of a series of presentations, introduced by a panel and then thrown open for general discussion, on the following subjects: Monday, April 17, (i) thrombosis and embolism, (ii) common endocrine problems, (iii) oral treatment of diabetes. Tuesday, April 18, (i) jaundice (two sessions), (ii) hypertension (two sessions). Wednesday, April 19, antibiotic therapy. Thursday, April 20, (i) surgical film, (ii) asthma, chronic bronchitis and emphysema (two sessions). Friday, April 21, (i) skin disorders—out-patient demonstration, (ii) drug toxicity, (iii) peripheral vascular disease, (iv) cancer chemotherapy.

The course will also include two clinical sessions and one lecture by Professor E. G. L. Bywaters, of the Postgraduate Medical School, Hammersmith, and the Rheumatism Research Unit, Canadian Red Cross Memorial Hospital, Taplow, Guest Professor at the Royal Melbourne Hospital, as follows: Wednesday, April 19, 11 a.m., arthritis out-patients; Thursday, April 20, 11 a.m., orthopædic out-patients; Thursday, April 20, 5.15 p.m., lecture in the hospital main theatre.

On Wednesday afternoon the class will visit the Infectious Diseases Hospital at Fairfield.

The morning sessions will be from 9 a.m. to 12.30 p.m., and afternoon sessions from 2 p.m. to 5 p.m., with breaks for

morning and afternoon tea. Lunch will be available at the hospital and arrangements for parking cars will be announced later. The fee for the course is £9 9s., and enrolments should be sent by April 4 to the Committee at the address given below.

Demonstrations at the Eye and Ear Hospital.

All medical practitioners are invited to attend without fee the following demonstrations on Saturday, April 22, which the honorary staff will conduct at the Royal Victorian Eye and Ear Hospital.

Eye: 9.30 a.m., clinical demonstration of common ocular diseases, Dr. Ronald Lowe; 11.15 a.m., illustrated lecturette on common ocular conditions, Dr. F. Fenton.

Ear, Nose and Throat, 9.30 a.m.: Mr. C. Cantor, (*a*) Ear, nose and throat cases of interest to general practitioners, (*b*) transparencies illustrating ear, nose and throat cases; Mr. Roy Stevens, (*a*) antrum washout—demonstration of technique, (*b*) illustrative ear, nose and throat cases; Dr. Constance Napier, (*a*) methods used in evaluation of deafness, (*b*) the importance of adenoidectomy in treatment of deafness in children—operative demonstration; Dr. Sol Brand, allergy cases relevant to ear, nose and throat; Dr. J. J. Billings, general medical cases relevant to the specialty.

Overseas Visitors.

Professor John T. Ingram, Professor of Dermatology, University of Durham, will lecture on "Colour in the Skin" at the Medical Society Hall at 8.15 p.m. on Friday, April 21. He will also visit hospitals during his stay in Melbourne. The fee for the abovementioned lecture is 15s., but those who have paid an annual subscription to the Committee are invited without further fee.

Dr. E. Harry Botterell, M.D., neurosurgeon at the Toronto General Hospital, will visit Melbourne for three or four weeks from April 20. Details of his programme will be announced later.

Professor Niilo Hallman, Professor of Pædiatrics, Helsinki, Finland, Pfizer Lecturer to the Australian Pædiatric Association, will visit the Royal Children's Hospital, Melbourne, from April 24 to 29.

Professor Douglas Hubble, Professor of Pædiatrics, University of Birmingham, will be a Guest Professor at the Royal Children's Hospital from approximately April 27 till May 13. He will lecture for the Committee at 8.15 p.m. on Thursday, May 4, on a subject to be announced.

Professor Bradley M. Patten, of the Department of Anatomy, University of Michigan, U.S.A., will visit Melbourne for a few days, probably in early May. Discussions will be arranged with anatomists and specialist cardiologists.

Courses for Higher Qualifications.

A course in microbiology, suitable for candidates for Part I M.D. and Part II of M.S., M.G.O. and the diplomas, will commence at the Bacteriology Department, University of Melbourne, at 2 p.m. on April 4, and will continue at that time for 20 weeks. The fee is £10 10s., and enrolments should be sent to the Committee by March 21.

Lectures in ophthalmology and special pathology, conducted by the Victorian Section of the Ophthalmological Society of Australia (B.M.A.), will commence on April 10. There will be approximately 80 lectures, in the late afternoons, conducted at the Eye and Ear Hospital. The fee is £31 10s., and should be sent to the Committee with the enrolment, on their special form, by March 27. This course will be suitable for candidates for D.O. Part II.

Lectures in radiodiagnosis, conducted by the Committee in consultation with the College of Radiologists of Australasia, will commence on Monday, May 1, at 4.30 p.m., and continue on Mondays and Thursdays for about 12 weeks. Enrolments, accompanied by the fee of £21, should be sent to the Committee by April 14. This course is suitable for candidates for the University and College diplomas.

Country Courses.

Courses for country practitioners will be conducted as follows:

Wangaratta.—On Saturday, April 8, in the Blood Bank Waiting Room of the Wangaratta Hospital, the following course will be held: 2.15 p.m., "Orthopædic Deformities in Children", Mr. Eric Price; 3.15 p.m., "Medico-Legal Aspects of Practice", Dr. Keith Bowden; 4.45 p.m., "Head Injuries", Mr. Keith Bradley. Dr. M. Rohan, 18 Docker Street, Wangaratta, is the local secretary.

Warracknabeal.—On Saturday, April 15, in the Nurses' Lecture Room, Warracknabeal Hospital, the following course will be held: 2 p.m., "Migraine and Vertigo", Dr. J. Billings; 3.15 p.m., "Analgesia and Anæsthesia in Childbirth", Dr. K. McCaul; 4.45 p.m., "Medico-Legal Aspects of General Practice", Dr. J. Birrell. Dr. Frank Kenny, Warracknabeal, is the local secretary for this course.

Fees.—The fees for these two courses are at the rate of 15s. per lecture, but those who have paid an annual subscription to the Committee are invited without further charge.

Albury.—On Saturday and Sunday, April 29 and 30, in the Nurses' Recreation Hall, Albury Base Hospital, the following course will be held: Saturday: 2 p.m., registration; 2.30 p.m., "Cerebral Vascular Disease", Dr. A. C. Schwieger; 4 p.m., "Cervical Spondylosis", Dr. A. C. Schwieger. Sunday: 10 a.m., "Indigestion and Chest Pain", Dr. Luke Murphy; 11.30 a.m., "Chronic Leg Ulceration", Mr. Allan Beech.

The secretary for this course is Dr. H. N. Meers, 1080 Waugh Road, North Albury. The Post-Graduate Committee in Medicine in the University of Sydney is conducting the course, and fees are payable to it. Those who have paid an annual subscription to the Melbourne Medical Post-Graduate Committee are invited without further charge.

Flinders Naval Depot.

At Flinders Naval Depot on Wednesday, May 12, at 2.30 p.m., Dr. Murray Maxwell will speak on "Nephritis". This lecture is given by arrangement with the Royal Australian Navy.

Anæsthetists.

The State Committee of the Faculty of Anæsthetists is holding a two weeks' full-time course of lectures and demonstrations, commencing on July 3 at the Royal Australasian College of Surgeons, Spring Street, Melbourne. The fee of £10 10s., is payable to the Secretary of the College, to whom further inquiries should be addressed.

Address.

The address of the Melbourne Medical Post-Graduate Committee is 394 Albert Street, East Melbourne. Telephone: FB 2547.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Courses for General Practitioners, May, 1961.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that the following courses will be held in May, 1961:

Tutorials in Anæsthesia.

Through the courtesy of the Faculty of Anæsthetists of the Royal Australasian College of Surgeons, Professor T. Cecil Gray, Professor of Anæsthetics in the University of Liverpool and Sims Commonwealth Travelling Professor for 1961, will conduct tutorials at 2 p.m. on May 5, 8, 9 and 10 at the Sydney Hospital. These tutorials are open to all interested general practitioners, free of charge to members of the annual subscription course. Inquiries should be made to the Post-Graduate Committee in Medicine at the above address.

Week-End Course in Cardio-Pulmonary Diseases.

The Post-Graduate Committee in Medicine in the University of Sydney announces that a week-end course in cardio-pulmonary diseases will be held in the Thoracic Unit of the Royal North Shore Hospital on Saturday and Sunday, April 15 and 16, 1961, under the supervision of Dr. C. G. Bayliss. The programme is as follows.

Saturday, April 15: 9.30 a.m., "Ætiology and Diagnosis of the Acute Pneumonias", Dr. H. Maynard Rennie; 9.50 a.m., "Management of the Acute Pneumonia", Dr. James Isbister; 10.5 a.m., "Pneumonia in Infants", Dr. Clair Isbister; 10.20 a.m., "Non-Tuberculous Empyema", Dr. H. J. Richards; 10.40 a.m., discussion; 11.15 a.m., "Hypertension—Investigation", Dr. R. G. Epps; 11.30 a.m., "Hypertension—Management", Dr. Z. S. Freeman; 11.45 a.m., "Hypertension—New Hypotensive Drugs", Dr. D. S. Stuckey; 12 noon, panel discussion on hypertension, Dr. D. S. Stuckey, Dr. R. G. Epps, Dr. Z. S. Freeman; 1.30 p.m., panel discussion on tuberculosis, Dr. C. G. Bayliss, Dr. H. Maynard Rennie, Dr. Keith Harris, Dr. A. G. McManis, Dr. James Isbister, Dr. B. L. Geddes; 2.30 p.m., discussion; 3 p.m., resuscitation

(this will include demonstration of the management of cardiac arrest with and without opening the chest and a demonstration of mouth-to-mouth breathing), Dr. Ian Monk, Dr. H. J. Richards and Dr. Bruce Clifton.

Sunday, April 16: 9.30 a.m., "Bronchiectasis", Dr. A. G. McManis; 9.50 a.m., "X-ray Aspects of Bronchiectasis", Dr. E. W. Lee; 10.5 a.m., demonstration of physiotherapy in bronchiectasis, Miss Colleen Smith; 10.15 a.m., discussion; 10.25 a.m., "Hæmoptysis", Dr. B. L. Geddes; 10.45 a.m., discussion; 11.15 a.m., "Indication for Surgery in Congenital Cardiac Lesion", Dr. W. A. Seldon; 11.25 a.m., "Indication for Surgery in Mitral Valve Lesion", Dr. R. G. Epps; 11.35 a.m., "Indication for Surgery in Aortic Valve Lesion", Dr. D. S. Stuckey; 11.45 a.m., "New Techniques in Cardiac Surgery", Dr. Ian Monk; 11.55 a.m., panel discussion, Dr. D. S. Stuckey, Dr. R. G. Epps, Dr. W. A. Seldon and Dr. Ian Monk.

The fee for attendance is £3 3s., and those wishing to enrol should make early written application, enclosing remittance, to the Course Secretary, the Post-Graduate Committee in Medicine, Herford House, 188 Oxford Street, Paddington, New South Wales. Telephone: FA 0671. Telegraphic Address: "Postgrad Sydney".

Week-End Course in Rheumatic Diseases.

The Post-Graduate Committee in Medicine in the University of Sydney announces that the dates of the week-end course in rheumatic diseases has been changed from early June to April 22 and 23, 1961. The guest speaker will be Professor E. G. L. Bywaters, Honorary Director of the Rheumatism Research Unit and Honorary Consultant Physician to the Canadian Red Cross Memorial Hospital, Taplow, England. Professor Bywaters will speak on "Vascular Lesions in Connective Tissue Disease" and "Joint Lesions in Bone Disease". The course will be held at the Royal Prince Alfred Hospital, from 2 p.m. to 5 p.m. on Saturday, April 22, and from 9.30 a.m. to 5 p.m., on Sunday, April 23. A detailed programme will be available shortly. The fee for attendance is £3 3s., and those wishing to attend should make enrolment with the Course Secretary, Post-Graduate Committee in Medicine, Herford House, 188 Oxford Street, Paddington, New South Wales, at an early date. Telephone: FA 0671. Telegraphic Address: "Postgrad Sydney".

Seminars on Pulmonary Heart Disease.

The Post-Graduate Committee in Medicine in the University of Sydney has arranged the following seminars on pulmonary heart disease, as the first in the 1961 series of evening seminars dealing with various aspects of cardio-vascular diseases to be held in the Maitland Lecture Hall, Sydney Hospital, under the joint supervision of Dr. G. E. Bauer and Dr. J. G. Richards. The programme is as follows.

Wednesday, April 5, "Pulmonary Embolism": 8 p.m., "Physiology of Pulmonary Embolism", Dr. D. F. J. Halmagyi; 8.30 p.m., "Clinical Features of Pulmonary Embolism", Dr. F. L. Ritchie; 9 p.m., "Diagnostic Aids in Pulmonary Embolism", Dr. G. E. Bauer; 9.30 p.m., panel discussion.

Wednesday, April 12, "Emphysema and Heart Failure": 8 p.m., "Clinical Aspects of Chronic Bronchitis, Emphysema and Heart Failure", Dr. W. G. Telleson; 8.30 p.m., "Physiological Disturbances in Emphysema", Dr. H. J. H. Colebatch; 9 p.m., "Management of Chronic Pulmonary Heart Disease", Professor R. B. Blacket; 9.30 p.m., panel discussion.

Wednesday, April 19, "Pulmonary Hypertension": 8 p.m., "Ætiology, Symptomatology, Diagnosis and Management of Pulmonary Hypertension", Dr. H. P. B. Harvey, Dr. J. B. Hickie and J. G. Richards; 9.30 p.m., panel discussion.

Wednesday, April 26, "Respiratory Function": 8 p.m., "Introduction to Respiratory Function", Dr. John Read; 8.30 p.m., film, "Principles of Respiratory Mechanics"; 9.30 p.m., question time.

The inclusive fee for attendance is £2 2s., and those wishing to enrol are requested to make early written application, enclosing remittance, to the Course Secretary, Post-Graduate Committee in Medicine, Herford House, 188 Oxford Street, Paddington, New South Wales. Telephone: FA 0671. Telegraphic Address: "Postgrad Sydney".

General Revision Course.

The Post-Graduate Committee in Medicine in the University of Sydney announces that the annual general revision course will be held in Sydney for two weeks beginning on May 8, 1961. As in previous years, the main emphasis is on therapeutics, and the programme is a comprehensive survey of modern trends in diagnosis and treatment of special value to general practitioners. The Post-Graduate Medical Foundation has made available ten Upjohn grants to medical practitioners to attend the course. Unless otherwise indicated, the course will be held in the Nurses' Lecture Theatre of the Royal Hospital for Women, Paddington. The Lecture Theatre is situated in the basement of the Nurses' Home, on the right-hand entrance of Glenmore Road. Cars may be parked conveniently in Glenmore Road and in Brown Street. Limited accommodation is available at the hospital for six male and six female medical practitioners at a cost of £3 16s. 7d. per week. Early application is essential and should be made to the Post-Graduate Committee. The programme is as follows.

Monday, May 8, Nurses' Lecture Theatre, Royal Hospital for Women: 9.15 a.m., registration. 9.45 a.m., opening of course by Mr. C. A. Hardwick, President of the Benevolent Society of New South Wales. 9.55 a.m., welcome and review of course by Dr. V. M. Coppleson, Chairman of the Post-Graduate Committee in Medicine. 10.35 a.m., symposium, "The Place of Steroids in Modern Medicine": chairman, Dr. Douglas Anderson; panel, Dr. T. I. Robertson, Dr. Ralph Reader, Dr. John McDonald. 11.45 a.m., symposium, "Infectious Hepatitis": chairman, Dr. C. J. Cummins; "Epidemiology", Dr. J. J. Donnellan; "Clinical Manifestations and Treatment", Dr. Stanley Goulston; "The Viewpoint of the General Practitioner", Dr. J. G. Radford; discussion. 2.15 p.m., symposium, "Common Skin Diseases in General Practice": chairman, Dr. E. Murray-Will; "Treatment of Keloids and Hæmangiomas", Dr. J. C. Belisario; "Chronic Discoid Lupus Erythematosus", Dr. F. J. Collett; "Management of Paronychia", Dr. L. J. Cains; "Finding the Cause of Contact Dermatitis", Dr. Brian McGaw; "Drug Eruptions", Dr. R. H. King; discussion and question time.

Tuesday, May 9, Nurses' Lecture Theatre, Royal Hospital for Women: 9.15 a.m., symposium, "Obstetrical Problems in General Practice": chairman, Professor Bruce T. Mayes; "Accidental Hæmorrhage", Dr. Elton Holman; "Severe Preeclampsia and Eclampsia", Dr. Reginald Bowman; "Postpartum Hæmorrhage", Dr. W. J. Garrett; questions. 2.15 p.m., symposium, "Gynæcological Problems in General Practice": chairman, Dr. George Stening; "The Valuation of Cancer Detection", Dr. Mary Heseltine; "Carcinoma in Situ and its Treatment", Dr. James Furber; "Ovarian Cysts", Dr. Kelvin McGarrity; discussion.

Wednesday, May 10, Nurses' Lecture Theatre, Royal Hospital for Women: 9.15 a.m., "Ear, Nose and Throat in General Practice", Dr. Harry D. Raffan. 10.45 a.m., "Ophthalmology in General Practice", Dr. John Antill Pockley. 11.45 a.m., "Alcoholism", Dr. S. J. Minogue. Free afternoon; this has been kept aside for private arrangements and other specially arranged activities. A choice is offered to members to visit the following: 1.30 p.m., luncheon at the Commonwealth Rehabilitation Centre, "Mt. Wilga", Hornsby, followed by inspection of the work of the Centre; discussion; afternoon tea; transport will be arranged; 2.30 p.m., Isotope Laboratory, St. Vincent's Hospital, Victoria Road, Darlinghurst; 2.30 p.m., Australian Atomic Energy Commission Research Establishment, Lucas Heights. Strictly limited to 24. Special application form must be obtained from the Post-Graduate Committee. Closing date for applications is April 28.

Wednesday, May 10, Stawell Hall, 145 Macquarie Street, Sydney: 8.15 p.m., "Breast Diseases in General Practice", Dr. Hedley Atkins, Surgeon to Guy's Hospital, London, and Sims Commonwealth Travelling Professor for 1961.

Thursday, May 11, Nurses' Lecture Theatre, Royal Hospital for Women: 9.15 a.m., "The Relationship of Doctors to their Colleagues and their Patients", Dr. G. L. Howe. 10.45 a.m., symposium, "Orthopædic Problems in General Practice": chairman, Dr. N. H. Morgan; "Neck and Shoulder Pain", Dr. Cecil Langton; "The Use of Cortisone", Dr. Denis Rowe; "Treatment of Common Fractures", Dr. N. H. Morgan; "Common Tendon Injuries", Dr. Collins Greaves; "Backache", Dr. Richard Hodgkinson; discussion.

Thursday, May 11, Broughton Hall Psychiatric Clinic, Leichhardt: 2.15 p.m., demonstration of psychiatric problems by Professor W. T. Trethowan and the staff.

Thursday, May 11, Great Hall, University of Sydney: 8.15 p.m., Fourteenth Annual Post-Graduate Oration, "George Bass", Dr. Keith Bowden, of Melbourne.

Friday, May 12, Nurses' Lecture Theatre, Royal Hospital for Women: 9.15 a.m., symposium, "Modern Methods in the Management of Cancer": chairman, Dr. K. W. Starr; "The Role of Surgery", Dr. R. P. Melville; "The Role of Radiotherapy", Dr. L. A. Atkinson; "The Role of Chemotherapy",

Dr. A. Freedman; discussion and question time. 10.45 a.m., "Drugs in the Treatment of Terminal Cancer", Dr. W. J. Moon, of the Austin Hospital, Melbourne. Afternoon: Post-Graduate Golf Match.

Saturday, May 13, Red Cross Blood Transfusion Centre, 1 York Street, Sydney: 9.15 a.m., demonstration of blood grouping, Rh testing and blood transfusion techniques, Dr. Hugh K. Ward and Dr. R. J. Walsh.

Monday, May 15, Nurses' Lecture Theatre, Royal Hospital for Women: 9.15 a.m., "The Management of Hypertension", Sir William Morrow. 10.45 a.m., "Coronary Disease", Professor R. B. Blacket. 11.45 a.m., symposium, "Management and Rehabilitation of Patients with Strokes": chairman, Dr. Laurence Hughes; panel, Dr. W. J. Burke and Dr. R. I. Meyers. 2.15 p.m., symposium, "Advances in Diseases of the Liver": chairman, Professor C. R. B. Blackburn; "Liver Function Tests", Dr. D. W. Piper; "Hepatitis and Chronic Liver Disease", Professor C. R. B. Blackburn; "Drug and Chemically Induced Liver Disease", Dr. J. G. Rankin; "Management of the Patient with Ascites", Dr. A. E. McGuinness; "Management of the Patient with Hepatic Failure", Dr. W. B. Hennessy; 4.25 p.m., discussion.

Tuesday, May 16, Main Lecture Theatre, Royal Alexandra Hospital for Children, Camperdown: 9.15 a.m., "Fits, Faints and Funny Turns", Dr. D. G. Hamilton. 10.30 a.m., "When to Consult the Pædiatric Surgeon about the Nervous System". Dr. M. Sofer Schreiber. 11.30 a.m., "Encopresis, Enuresis, Breath Holding and the Like", Dr. C. A. Rigg. 1 p.m., luncheon at Hospital Canteen at cost of 6s.; payment to be made to the Post-Graduate Committee. 2.15 p.m., "Points to Look for in the Newborn Infant" (with film "Resuscitation of the Newborn"), Dr. E. D. Burnard, Dr. F. L. Rothwell. 4 p.m., "Endocrine Disorders in Childhood", Professor Douglas Hubble, Professor of Pædiatrics and Child Health in the University of Birmingham.

Tuesday, May 16, Stawell Hall, 145 Macquarie Street, Sydney: 8.15 p.m., symposium, "What's New in Drugs and Therapeutics", chairman, Dr. C. G. McDonald; "Drug Management of Cardiac Arrhythmias", Dr. George Hall; "Treatment of Diabetic Coma", Dr. W. Wilson Ingram; "Modern Management of Peptic Ulcer", Dr. Stanley Goulston; "New Tranquillizers (including 'Tofranil' and 'Librium')", Professor W. H. Trethowan; question time.

Wednesday, May 17, Nurses' Lecture Theatre, Royal Hospital for Women: 9.15 a.m., panel discussion, "Therapeutics": chairman, Sir William Morrow; "The Endocrines", Dr. John Greenaway; "Treatment of Infections", Dr. R. S. Packard; "Respiratory Diseases", Dr. A. G. McManis; "Renal Diseases", Dr. James Isbister; discussion. 2.15 p.m., "Conditions Simulating Arthritis", Dr. Selwyn Nelson. 3.45 p.m., "Present Day Treatment of Diabetes", Dr. Keith Harrison.

Wednesday, May 17, Stawell Hall, 145 Macquarie Street, Sydney: 8.15 p.m., "Common Injuries in Sport", Dr. Hedley Atkins.

Wednesday, May 17, Main Lecture Theatre, Royal Alexandra Hospital for Children: 8.15 p.m., "Steatorrhœa in Children", Professor Douglas Hubble.

Thursday, May 18, Nurses' Lecture Theatre, Royal Hospital for Women: 9.15 a.m., "Scientific Feeding of Infants", Dr. Clair Isbister. 10.45 a.m., symposium, "Anæsthetics in General Practice": chairman, Dr. L. T. Shea; "Common Anæsthetic Difficulties", Dr. J. Loughman; "Deaths under Anæsthetics", Dr. Ross Holland; "Pædiatric Anæsthesia", Dr. George Lomaz; discussion. 2.15 p.m., symposium, "The Accident Case": chairman, Professor John Loewenthal; "Resuscitation", Professor Frank Rundle; "Head Injuries", Dr. W. Scott Charlton; "Thoracic Injuries", Dr. Harry Windsor; "Abdominal Injuries", Dr. Eric Goulston; discussion and question time; "Limb Injuries", Dr. John S. Roarty; "Vascular Injuries", Professor John Loewenthal; "Nerve and Tendon Injuries", Dr. D. Officer Brown; question time.

Thursday, May 18, Stawell Hall, 145 Macquarie Street, Sydney: 8.15 p.m., "Accident and Design in Surgery", Professor T. Cecil Gray, Professor of Anæsthetics in the University of Liverpool and Sims Commonwealth Travelling Professor for 1961.

Friday, May 19, Nurses' Lecture Theatre, Royal Hospital for Women: 9.15 a.m., question session, medical subjects: chairman, Dr. Cotter Harvey; panel, Dr. Innes A. Brodziak, Dr. Richard Harris, Dr. A. E. McGuinness, Dr. Justin Markell.

The fees are as follows: full course, £12 12s.; morning or afternoons only, £6 6s.; one week only, £6 6s. Early application, enclosing remittance, should be made to the Course Secretary, The Post-Graduate Committee in Medicine, Herford House, 188 Oxford Street, Paddington, New South Wales. Telephone: FA 0671. Telegraphic Address: "Postgrad Sydney". Fees and travelling expenses for this course are taxation deductions for those who are at present in practice. When such deductions are claimed, "Taxation File No. AF/1865" should be quoted.

Royal Australasian College of Surgeons.

ADMISSION OF NEW FELLOWS.

THE following, having satisfied the Court of Examiners, were admitted to Fellowship of the Royal Australasian College of Surgeons by the Council on February 18, 1961: John Bell, Ivan Cher, Thomas Joseph Connelley, Barry Desmond Cooke, John Yale Crooks, John Daniel Crowley, John Russell Dalton, Richard English Dunstan, William John Garrett, David Stuart Gibson, Peter Gibson, Richard Spencer Gye, Hugh Malcolm Hadley, Frank James Ham, David Howell, John Lister Colless Lahz, George Adrian Dickson Lamb, John Alastair McArthur, Geoffrey Murdoch McFadden, Edgeworth David McIntyre, Eric Vincent Mackay, Robert Gordon Mackay, Malcolm Benbow Menelaus, John David Henry Muir, Lawrence Septimus Parker, David Pfanner, Graeme James Pollock, Graham Raymond Albert Raad, Don Rabinov, John Frederick Sander, George Julius Schnitzler, John Ridley Solomon, Jack Sunderman, John Robert Thomson, James Geoffrey Toakley, John Paul Tonkin, Yuen Lin Tseng, Jack Upsdell, John Bernard Walker, Fergus Roy Wilson, Ronald Peter Yaxley, John Douglas Newman Yelland,

FACULTY OF ANÆSTHETISTS.

Admission of New Fellows.

THE following, having satisfied the Court of Examiners were admitted to Fellowship of the Faculty of Anæsthetists, Royal Australasian College of Surgeons, by the Council on February 18, 1961: Garvan John Carroll, Harold Wah Kim Chan, Richard Hugh Shepherd Connock, Barbara Phyllis Coppen, Henri René Paul Coutanceau, John Davenport, Frank Fisher, John Francis Anning Forster, Robert Mercer Hart, Newton Potter, Bryan Edmund Sharkey, John Graham Stocks, Ian Archibald Waldie.

Australian College of General Practitioners.

QUEENSLAND FACULTY.

Post-Graduate Week-End, Surfers' Paradise.

THE Queensland Faculty of the Australian College of General Practitioners is holding its Pfizer Post-Graduate Week-End at Surfers' Paradise on the Queensland Gold Coast from April 28 to 30, 1961. The week-end is open to all medical practitioners, and a special invitation is extended to interstate visitors. Accommodation is available at the Chevron Hotel, Surfers' Paradise, but members may stay elsewhere if they so desire. If accommodation is required, it will be arranged by the Secretary on request. The fee for the course and social functions is £9 9s., and includes wives and husbands. All who propose to attend are asked to advise the Secretary, Box 1498V., G.P.O., Brisbane. The programme for the week-end is as follows:

Friday: 8 p.m., Informal evening party and registration, Chevron Hotel.

Saturday: 9.15 a.m., Official opening and registration, Paradise Room, Surfers' Paradise Hotel; opening address by the Queensland Director-General of Health, Dr. A. Fryberg, M.B.E.; 9.45 a.m., "The External Ear", Dr. Colin Wark, M.B.E., otorhinolaryngologist; 11 a.m., "Prevention

of Disabilities following Parturition", Dr. Arthur Hill, Melbourne (guest lecturer); 2 p.m., panel discussion, "Goitre"—Dr. A. W. Steinbeck, physician, Dr. Kevin Mead, radiotherapist, Dr. J. H. Little, surgical pathologist, Dr. C. Leggatt, M.B.E., general surgeon, Dr. K. Aaron, moderator; 3.45 p.m., "What Causes the Uterus to Contract?", Professor R. W. Hawker, physiologist.

Sunday: 9.15 a.m., "Orthopædics of the Upper Limb", Dr. M. Gallagher, orthopædic surgeon; "Neuro-Surgical Emergencies", Dr. K. Jamieson, neurosurgeon; 11.15 a.m., "Post-Menopausal Bleeding", Dr. Arthur Hill, Melbourne; 2 p.m., "Surgery of Peripheral Arterial Disease", Dr. S. Mellick, general surgeon; 2.45 p.m., "The Ocular Fundus in Health and Disease", Dr. Daniel Hart, ophthalmic surgeon; 3.45 p.m., quiz session—(*a*) "Prophylactic Antimicrobials", (*b*) "Steroids", (*c*) "Anticoagulants"; panel, Dr. Arthur Hill, Dr. A. W. Steinbeck, Dr. S. Mellick, Dr. D. Hart.

Notes and News.

Pocket Radio Receivers for "On Call" Hospital Personnel.

The use of small two-way pocket radio receivers has given "on call" hospital personnel at a number of American hospitals greater freedom in the use of their time away from the hospital, and has eliminated having to report in by telephone at regular intervals. Designed by General Electric Company (U.S.A.), the new system equips staff members with a voice communications receiver weighing 10 oz., through which the hospital can make contact with them in a second. The unit allows laboratory, blood-bank and X-ray technicians, as well as nurses, anæsthetists and physicians, to be "in touch" with their hospital, even if they are on beaches or other places where there are no telephones. The units, which may be placed on the front seat of a motor car, worn clipped to a belt or in a leather case on a shoulder strap, are known officially as voice directors, but grateful hospital staff members refer to them as "liberators". Messages are sent over a large transmitter-receiver unit at the hospital, which serves as a base station. This is operated 24 hours a day, either by the telephone switchboard operator or by nurses on duty. Each staff member is assigned a call number. He responds only to messages directed to him, and either telephones the hospital or goes there at once. The system also has been extended to include standard type two-way radios installed in the cars of staff physicians. The same hospital base station transmitter is used for the vehicular network. The use of the two-way radio system enables doctors, driving to the hospital, to relay emergency instructions to hospital nurses and other special personnel.

Fourth World Congress of Cardiology.

The Fourth World Congress of Cardiology will be held in Mexico City from October 7 to 13, 1962. Further details and registration forms may be obtained from the Secretary, Dr. I. Costero, Mexico City, Mexico 7, D.F.

Naval, Military and Air Force.

APPOINTMENTS.

THE following appointments, changes, etc., are published in the *Commonwealth of Australia Gazette*, No. 19, of February 23, 1961.

ROYAL AUSTRALIAN AIR FORCE.

Permanent Air Force.

Medical Branch.

The probationary appointment of each of the following Flight Lieutenants is confirmed:—T. T. Pietzsch (0218354), C. F. Allardyce (0218325), J. T. Cummins (0312881), A. V. L. Hill (036613), J. A. Davidson (019689).

Squadron Leader G. C. Nelsen (018487) is granted special leave without pay from 24th November, 1960, to 23rd May, 1961, inclusive.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED FEBRUARY 18, 1961.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	..	2(1)	..	..	..	..	..	2
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	6	..	1(1)	..	..	..	4	..	11
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	2(1)	1	..	..	..	..	..	..	3
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	1	13(13)	5(3)	..	..	..	7	..	26
Diphtheria	..	..	..	..	..	..	..	..	..
Dysentery (Baciliary)	..	1(1)	1(1)	1(1)	..	..	..	..	3
Encephalitis	..	2(1)	..	..	..	..	..	..	2
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	1	..	..	1
Infective Hepatitis	139(63)	62(36)	26(6)	48(15)	9(8)	8	2	3	297
Lead Poisoning	..	..	..	..	1(1)	..	..	..	1
Leprosy	..	..	..	..	..	..	10	..	10
Leptospirosis	..	1	..	..	..	..	..	..	1
Malaria	..	1(1)	..	..	..	..	..	..	1
Meningococcal Infection	1(1)	..	..	..	..	..	..	..	1
Ophthalmia	..	..	..	..	..	..	..	1	1
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	2	..	..	..	2
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	1	2(2)	..	..	..	1	..	..	4
Puerperal Fever	7	..	..	..	..	..	..	..	7
Rubella	..	4(4)	..	..	13(12)	..	..	..	17
Salmonella Infection	..	..	..	..	1(1)	..	..	..	1
Scarlet Fever	3	4(1)	..	..	1(1)	..	..	1	9
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	1(1)	..	..	..	1
Trachoma	..	..	..	..	..	..	3	..	3
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	43(31)	8(4)	19(4)	2(2)	7(5)	..	..	..	79
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

The following appointments, changes, etc., are published in the *Commonwealth of Australia Gazette*, No. 21, of March 2, 1961.

NAVAL FORCES OF THE COMMONWEALTH.

Permanent Naval Forces of the Commonwealth (Sea-Going Forces).

Honorary Physician.—Surgeon Commander Benjamin Crawshaw, D.S.C., is appointed Honorary Physician to His Excellency the Governor-General, dated 14th October, 1960.

Termination of Appointments.—The appointments of John Francis Killick and Alan John Lyne as Surgeon Lieutenants (for Short Service) are terminated, dated 20th November, 1960.

Citizen Naval Forces of the Commonwealth.

Royal Australian Naval Reserve.

Termination of Appointments.—The appointments of the following are terminated:—Surgeon Lieutenants Peter William Fay, Ronald Antony Harrison, Peter Arundel Johnson and Alan Thomas Rose, dated 29th August, 1960; Surgeon Lieutenant David Darnton Watson, dated 6th September, 1960; Surgeon Lieutenant David Robert Holden Kennedy, dated 20th October, 1960.

Corrigendum.

QUADRUPLE ANTIGEN.

WE have been requested by the Commonwealth Serum Laboratories to make a correction to the statement on quadruple antigen which was published in the issue of March 4, 1961, on page 348. The correction relates to the storage conditions of the vaccine and should read:

32° F.-36° F.—3 months. 37° F.-43° F.—2 months. 44° F.-50° F.—6 weeks. 75° F.—one week. 98° F.—2 days.

The article indicates that quadruple antigen has lost half its potency after six months' storage at 44° F.-50° F. This is incorrect and should read six weeks. This error was contained in the original leaflet but it has subsequently been amended.

Nominations and Elections.

THE undermentioned have been elected as members of the New South Wales Branch of the British Medical Association: Everett, Ian Alexander, M.B., B.S., 1961 (Univ. Sydney); Harrison, Owen Michael, M.B., B.S., 1959 (Univ. Sydney); Kardos, Ida Magdalena, M.D., 1927 (Univ. Pecs), (registered under Section 17 (2A) of the Act); Lloyd, Bruce Logan, M.B., B.S., 1960 (Univ. Sydney); Moran, Clement Charles, M.B., B.S., 1959 (Univ. Sydney); Morgan, Bruce Alexander, M.B., B.S., 1956 (Univ. Sydney); Nixon, Peter Frank, M.B., B.S., 1961 (Univ. Sydney); Sertori, Joseph Gerard, M.B., B.S., 1957 (Univ. Sydney).

Deaths.

THE following deaths have been reported:

THOMPSON.—Geoffrey Ashburton Thompson, on March 2, 1961, at Perth.

JULL.—Roberta Henrietta Margaretta Jull, on March 6, at Perth.

LLOYD.—Charles Humphrey Lloyd, on March 11, 1961, at Inglewood, N.S.W.

STEWART.—James Stewart, on March 13, 1961, at Maitland, New South Wales.

HOETS.—John William van Rees Hoets, on March 17, 1961, at Sydney.

Diary for the Month.

MARCH 28.—New South Wales Branch, B.M.A.: Council (Election of Officers).
MARCH 30.—South Australian Branch, B.M.A.: Scientific Meeting.
APRIL 4.—New South Wales Branch, B.M.A.: Organization and Science Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

Authors of papers are asked to state for inclusion in the title their principal qualifications as well as their relevant appointment and/or the unit, hospital or department from which the paper comes.

References to articles and books should be carefully checked. In a reference to an article in a journal the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

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